AN OPEN NON RANDOMIZED CLINICAL TRIAL OF KALINGATHI ENNAI IN SOOTHAGA VAAYU (POLYCYSTIC OVARIAN SYNDROME)

The dissertation submitted by

Dr. S. BRUNDA (Reg. No. 321511102)

Under the Guidance of

Prof. Dr. K. KANAKAVALLI, M.D.(S)

Submitted to

THE TAMIL NADU DR. M.G.R. MEDICAL UNIVERSITY

In partial fulfillment of the requirements
For the award of the degree of

SIDDHA MARUTHUVA PERARIGNAR

DOCTOR OF MEDICINE (SIDDHA)

BRANCH I – MARUTHUVAM

POST GRADUATE DEPARTMENT OF MARUTHUVAM

THE GOVERNMENT SIDDHA MEDICAL COLLEGE

CHENNAI – 106

OCTOBER - 2018

CERTIFICATE

This is certify that the dissertation entitled **"AN OPEN NON-RANDOMIZED CLINICAL TRIAL OF KALINGATHI ENNAI IN SOOTHAGA VAAYU (POLY CYSTIC OVARIAN SYNDROME)"** is a bonafide work done by **Dr**. **S. BRUNDA,** Government Siddha Medical College, Chennai – 600106 in partial fulfillment of the University rules and regulations for award of **SIDDHA MARUTHUVA PERARIGNAR** under my guidance and supervision during the academic year 2015 -2018.

Name & Signature of the Guide

Name & Signature of the HOD

Name & Signature of the Principal

AN OPEN NON RANDOMIZED CLINICAL TRIAL OF KALINGATHI ENNAI IN SOOTHAGA VAAYU (POLYCYSTIC OVARIAN SYNDROME)

The dissertation submitted by

Dr. S. BRUNDA (Reg. No. 321511102)

Under the Guidance of

Prof. Dr. K. KANAKAVALLI, M.D.(S)

Submitted to

THE TAMIL NADU DR. M.G.R. MEDICAL UNIVERSITY

In partial fulfillment of the requirements
For the award of the degree of

SIDDHA MARUTHUVA PERARIGNAR

DOCTOR OF MEDICINE (SIDDHA)

BRANCH I – MARUTHUVAM

POST GRADUATE DEPARTMENT OF MARUTHUVAM

THE GOVERNMENT SIDDHA MEDICAL COLLEGE

CHENNAI – 106

OCTOBER - 2018

ACKNOWLEDGEMENT

ACKNOWLEDGEMENT

I express my elegance to the God for giving me the opportunity to do this dissertation work.

I thank to the Siddhars for their blessings and guidance to me to complete this dissertation work successfully.

I express my cordial and sincere thanks to respected **Prof. Dr.P. Parthibhan, M.D.(S),** Joint Director, Indian Medicine and Homeopathy, Chennai-106, for his valuable guidance, concern suggestion, inspiration and encouragement throughout the course of this study.

I sincerely thank to respected **Prof. Dr.K. Kanakavalli, M.D.(S),** Principal and my Guide, Government Siddha Medical College, Chennai-106, for her excellent guidance, inspiration and encouragement, right from the time of choosing this topic to submitting this dissertation book with perfection.

I sincerely thank to respected **Prof. Dr.N. Anbu, M.D.(S),** Head of the Department, Post Graduate (Pothu Maruthuvam), Government Siddha Medical College, Chennai-106, for his necessary advice at every step of my dissertation work, valuable suggestions, and provided very good command during this study.

I also extend my thanks to **Dr.U. Chithra, M.D. (S),** Asst. Lecturer, for her valuable guidance, hopeful support for completion of my whole study.

I wish to express my thanks to **Dr.R. Menaka, M.D. (S),** Asst. Lecturer, for her support and suggestion during the period of my study.

I wish to express my sincere thanks to **Dr.S.M. Chitra, M.D. (S),** Asst. Lecturer, for her kind opinions in this dissertation work.

I am very glad to thank **Dr.R. Sasirekha, M.D. (S),** Asst. Lecturer, for her kind opinions in this dissertation work.

I would like to express my thanks to **Mr.K.N. Sunil kumar** , R.O and HOD, Department of pharmacognosy, C.C.R.S,Chennai -106 for authenticating drugs.

I also convey my sincere thanks to **Dr.P. Muralidharan, M.Pharm, Phd**, HOD ,Department of Pharmacoloy, C.L.Baid Metha college of Pharmacy, Thuraipakkam, Chennai , for doing my pre-clinical studies for my trial medicine.

I also thankful to **Mr. Selvaraj, HOD**, Biochemistr dept, and Lab Assistant Mrs. Shanthi for doing my Biochemical Analysis.

I deeply convey my gratitude to **Dr. Sathiya Rajeswaran, M.D.(S), R.O, C.C.R.S,** Chennai-106 for his moral and timely support during my work.

I thank Librarian **Mr. V. Dhandayuthapani, M.Com, M. Lib (Sci),** Dr. Ambedkar Library, GSMC, Chennai.

I would like to thank all the teaching staffs of PG department, Govt. Siddha Medical College, Chennai – 106 for their timely suggestion and encouragement.

I like to thank **all patients** for eagerly accepting themselves and gave a full support for completes the study.

I like to thank my parents **Mr. V. Sivanandam, Mrs.G.S. Sasikumari** and my beloved sisters **S.Hari preetha and S.Boojiya sree** for motivating and encouraging me in all circumstances.

Finally I would like to thank all of **my friends and batchmates** for their kind support and co-operation.

My deepest gratitude goes to my friend **Dr.M.Veerasivaraman** & beloved sisters **Dr. A. Kavinilavu, Dr. K. Dhivyalakshmi & Dr. K. Sowmiya** for their unforgettable help during my project.

CONTENTS

CONTENTS

INTRODUCTION

INTRODUCTION

Siddha system of medicine is the ancient, unique, potent, and holistic medical system among all the systems of medicine in the world. It is a traditional system of healing that originated in south India, which flourished between 2500BC and 1700AD[(1)]. Generally, origin of this system is associated with Siddhars, the ascetics who aimed for ageless body to achieve their highest spiritual goal. Prevention and cure are the basic aims of all systems of medicine whereas the Siddha system has in addition the transcendental motivation of what might be called the immortality of the body.

Siddha system firmly believes that whatever changes which occurs in the world around us (Macrocosm- Andam) is certain to create an impact on the health of a man (Microcosm). So if any alteration in nature of macrocosm (Universe World) spontaneously affect the human body function. This concept of Siddha medicine could be rightly considered as the pioneer efforts of environmental protection for a healthy living.

Siddha concepts are mainly based on panchabootha theory. According to panchabootha hypothesis the Universe originally consisted of atoms which contributed to five basic elements. They are Earth, Water, Fire, Air and Space, which were corresponded to the five senses of human body and they were the fundamentals of all the corporal things in the World[(2)]. This five elements combine to form the Tridoshas or humours whose balance is essential for the maintenance of health.

Apart from this, Siddha system of medicine consists of three humours namely Vatham, Pitham and Kabham which normally exist in the ratio of 1:1/2:1/4. Derangement of the ratio in these humours lead to vatha, pitha and kabha diseases[(3)].

The anatomical, physiological and psychological functions of the body are known to be intricately and inherently connects as all of them emerge from the five elements. The structural components or the tissue components of the body are composed of seven types of materials called Udalthathus or Udalkattukal. If one thathu is defective, each connected thathu is affected, thereby triggering a chain

reaction of impairment at times throughout the entire tissue system. The formation of the thathus is through the food substances. The use of healthy foods is essential for sustaining the thathus.

The classical Siddha literature Aathmaratchamirtham Ennum Vaithiya Sangiragam quoted about Soothaga vaayu. The clinical features of Soothaga vaayu may be correlated with PCOS in modern aspects. Siddha literature pararasasekaram cite that any imbalance in three humours may inhibit the release of ovum from the ovaries. This may be related to the PCOS due to hormonal imbalance.

கேளுமே சூதகத்திலக்கினிவாயு

கெடுத்துவிடும் மாதவிடாய் கட்டிப் போகும்

-ஆத்மரட்சாமிர்தம் என்னும் வயித்திய சங்கிரகம்

PCOS is a heterogenous, multisystem endocrinopathy in women of reproductive age with various metabolic disturbances and a wide spectrum of clinical features such as menstrual abnormalities, obesity, and hyperandrogenism. This disease was discovered by and named as Stein-Leventhal syndrome in 1935. It has been attributed to several causes including change in lifestyle, diet and stress.

Current incidence of PCOS (5-6%) is fast increasing lately due to change in the lifestyle and stress. It is also becoming a common problem amongst adolescent, developing soon after puberty. Amongst infertile women, about 20% is attributed to anovulation caused by PCOS. The World Health Organization estimates that PCOS affects 116million women worldwide (3-4% of the people in the world)[(4)]. PCOS produces symptoms approximately in 5-10% of women during the reproductive age (12-45 years)[(5)].

Although several medications and treatment methods are available in modern medical field prevalence of PCOS is still uncontrollable in reproductive women due to lifestyle changes, diet and stress. Proper medication with lifestyle changes can decrease the occurrence of PCOS in women.

Having completely convinced with the literary evidences available in Siddha medicine, I have chosen Soothaga vaayu as my dissertation work which correlates with Poly cystic ovarian syndrome (PCOS) as described in the modern medical system.

KALINGATHI ENNAI is a herbal formulation mentioned in Siddha text Sikitcharatna Deepam Irandam Pagamagiya Vaithiya Chinthamani is indicated as an effective medicine for SOOTHAGA VAAYU (PCOS). Siddha system of treatment consist 32types of internal medicine and 32types of external medicine. Ennai (Medicated oil) is one among the 32 types of internal medicine. Medicated oils are classified into twelve types based on origin and five varieties by the mode of applications. As Kalingathi ennai is given internally it comes under Kudi ney. The active principles of the medicine get dissolved in the oil and it is absorbed depending upon administration.

On the whole as a compound medicine KALINGATHI ENNAI may be an effective, easy available with more potency and lesser side effects in the treatment of SOOTHAGA VAAYU.

In recent days, reproductive age group women's expects relief without any adverse effects for this disease. So I believed that the Siddha medicine Kalingathi ennai gives the best solution in Soothaga vaayu. Treatment is arrived for restoring balance to the mind and body system. Diet, lifestyle, asanas and meditation are advised to the patients, which play a major role not only in maintaining health but also in curing disease[(6)].

So I preferred to select Soothaga vaayu (Poly cystic ovarian syndrome) as the dissertation topic with the Siddha preparation Kalingathi ennai.

AIM
AND
OBJECTIVES

AIM AND OBJECTIVES

AIM:

The purpose of this study is to evaluate the safety and efficacy of Siddha herbal formulation *"*KALINGATHI ENNAI" in the treatment of SOOTHAGA VAAYU.

OBJECTIVES:

- Collections of various Siddha literature of the study.
- Herbal Identification and authentication of the trial medicine.
- To prepare the trial medicine *"*KALINGATHI ENNAI*"* as per Standard Operative Procedures medicine preparation.
- To study the evaluation of Siddha trial medicine "KALINGATHI ENNAI*"* for SOOTHAGA VAAYU.
- To evaluate the biochemical, physicochemical analysis of the trial medicine.
- To evaluate the safety profile like acute toxicity, sub acute toxicity of the trial medicine in animal models as per OECD guidelines 423&407.
- To evaluate the pharmacological analysis of OVULATION INDUCING ACTIVITY for my trial medicine.
- To correlate the Siddha aspects of SOOTHAGA VAAYU to POLY CYSTIC OVARIAN SYNDROME of Modern medicine with aspect of aetiology, classification, pathology, prognosis and clinical features.
- To gather the Siddha diagnostic parameters by Mukkutram, Udalthathukkal, Uyirthathukkal, and Envagai thervugal.
- To use modern parameters to confirm the diagnosis and prognosis of the disease.
- To make a clinical observation about the disease in relation of age, sex, occupation, socio economic status and diet.
- The haematological analysis, urine analysis, radiological studies and follicular studies will be done to all patients.
- All patients are subjected to thorough investigation before and after treatment.
- To find out the statistical analysis and efficacy of the trial medicine through clinical study.

REVIEW OF LITERATURE

SIDDHA ASPECT

REVIEW OF LITERATURE SIDDHA ASPECT

SOOTHAGA VAAYU

VERUPEYARGAL (SYNONYMS):

- Soothaga soolai
- Dhoora soolai
- Karpa vaayu

IYAL (DEFINITION):

A menstrual disease marked by pain at the epigastrium, corpulency, enlargement of the abdomen. It is due to the uterus being choked up with accumulation of the menses arising from heat combining with the deranged vayu in the system[7].

SOOTHAGAM UNDAGUM VITHAM:

“திங்களுறுமங்கையர்கள் கெற்பாசயமதை

தாங்கியிரு சிவிகையுண்டு

சிவிகையிரு பக்கமும் வீசியே

நிற்குமதினின்றொருகுழல் நரம்பு

பங்கமறவேயெழும் அடிவயிறு யோனியும்

சுற்றிப் பிணைந்து கொண்டு

பகருமதிலொரு முனை இரத்தாசயமதைக்

கவ்விக் குவிந்திருக்கும்

இங்கிதமதாகவே மறுமுனையது

அரிவையர் கெற்பாசயம் புகுந்து

இனிதாயரவினுட வாயளவாகவே

மூவிரலசைந்து நிற்கும்

மங்களமதாயிந்த நாதக்குழல்

வழி ரத்தாசயத்தினின்று

மறுவகலவே காரிரத்தம் சுரந்தினி

கெற்பாசயத்திலே தான்

நிதமுமிது தவறாது ஒரே துளிவிழும்

ஆறஞ்சதாம் நாளிலே

நேசமொரு குழல்வழி உருகியது வெளியிலே

பாயுமது யோனி வழியாய்

பதமாகவே சுகதேகியதுவாகிலொ

பூத்த முதல் மூன்று நாளும்

பகருதினி மோராற் கழஞ்சு நிறை பாயுமே

மேகமதினால் சூட்டினால்

இதமான வாயுவால் கிருமியின் ஏதுவால்

பூத்த பின் கணவனோடே

சேருவதினாலேயும் கடுநடைகளாலினி

சுமடு வெயில் தாக்குவதினால்

விதமான நாதமது கூடும் குறைந்திடும்

கெற்பமில்லாமலாகும்

விள்ளுமோராறு வகை வாயுவது

துதித்திடும் கேளு நீ ஓவ்வொன்றாய்”(8)

The physiology of women's menstrual cycle is illustrated in the Siddha literature magnificiently as before modern technologies had been developed. The uterus of women is attached to the ovaries with fimbria on either side through the fallopian tube.

The menstrual cycle for healthy women takes place with an interval of 30days. Endometrial shedding takes place for three days. The amount of blood lost per day in a cycle is calculated for a normal women is about 30.6 ml. (6 kazhanju- 6*5.1 = 30.6 ml)

NOI VARUM VAZHI (ETIOLOGY):

According to the text, Arivaiyar Chinthamani,

" மேகமதினால் சூட்டினால் இதமான வாயுவால்

கிருமியின் ஏதுவால் பூத்தபின் கணவனோடே

சேருவதினாலேயும் கடுநடைகளாலும் சுமடு வெயில் தாக்குவதினால்

விதமான நாதமது கூடும் குறைந்திடும் கெற்பமில்லாகும்"(9)

- Venereal diseases.
- Infections.
- Increased body heat due to excessive physical activity.
- Coitus at the time of menstrual cycle.

According to the text, Dhanvanthiri Vaithiyam (1st part),

"வஞ்சனை தன்னினாலும் மருந்தீடு தன்னினாலும்

மொஞ்சிடு சரீரவேட்கை யுறுதிசெய் தண்டிப்பாலும்

அஞ்சலாம் பிள்ளைப் பேறிலடங்கிய இரத்தத்தாலும்

மிஞ்சிய வாயுவாலுங் கருப்பநோய் மேவுமென்னே"(10)

- Diseases and food poisoning.
- Retention of lochia.
- Increased vayu produces uterine disorders.

According to the text, Agathiyar Kanma Kaandam 300,

"சுழலாமல் பெண்களுக்குக் கெற்பநோய் தான்

சூழ்ந்துவந்த கருமத்தைச் சொல்லக்கேளு

அழலாலே விந்துவகை யழித்தபாவ

மஞ்சாமற் பாலகனைக் கொன்றபாவம்

குழவியிளம் பிஞ்சுபூப்பறித்தபாவங்

கோவினங்கள் பருகும்பால் குடித்தபாவம்

விளைவான விளம்பயிரை யழித்தபாவ

மேதினியில் மலடான விந்தைதானே"(11)

SOOTHAGA VAAYU NOI KURIKUNANGAL (CLINICAL FEATURES):

கேளுமே சூதகத்தி லக்கினி வாயு

கெடுத்துவிடும் மாதவிடாய் கட்டிப் போகும்

ஆளுமே கருக்குழி தூர்ந்து தேகம்

அப்பனே உதிரமது அடிமூலத்தில்

நீளுமே சூதகத்தில் வாயு தோன்றி

நேரான அடிவயிறு வலிப்பு காணும்

பாளுமே தலைவலிக்கும் இடுப்புளைச்சல்

பக்குவமாய் மருந்துண்ண தீருந்தானே(12)

- Amenorrhoea due to accumulation of vaayu and agni in ovaries.
- Anovulation.
- Lower abdominal pain.
- Headache and Low back pain.
- Central obesity.

SOOTHAGA VAAYU IN VARIOUS SIDDHA TEXTS

(i) According to the text, Arivaiyar Chinthamani,

பாதமொடு சூதக வாயுவது தன்மை கேள்

மாதவிடையது குறையுமே

புகழுரிய வயிறு கனமாகியதி வேதனை

அடிவயிறு புண்போல நோவாம்

போதமுறு சென்னிவலி உச்சியதிலே குத்து

இரு கொங்கையது முளையுமே

மோதியதி தாயிரு கை கால் கடுக்குமே

கால் மண்ணையது முளையுமே

முதிய நாவானது வழுவழுப்பாயிடும்

அன்னம் குறைந்து வருமே

நீதமுறு மேனியது விளறுமதி சோபமாய்

சொற்பனம் அதிகரிக்கும்

நித்தனருள் பெற்றமுனி சொல்லு

முரையின்படி செந்தமிழாயுரைத்தேன்(13)

- Scanty menstruation.
- Lower abdominal pain.
- Pain in the breast.
- Pain in the upper and lower limbs.
- Loss of appetite.
- Excessive sleep.
- Head ache.
- Anaemia.
- Excessive sleep.

(ii) According to the text, Arivaiyar Chinthamani,

தானான சூதகத்தின் வாய்வின் தன்மை

தானே அக்கினி வாய்வு சூதகத்தில் தங்கி

மானே மாதவிடை கட்டிக் கொள்ளும்

மருவு சூதக நாளில் வாய்வுண்டாம்

தானாரே அடிவயறு புண்போல் நோகும்

தலைவலியுண்டாம் வயற்றில் நோவுண்டாகும்

ஆனாலும் வயறுடலும் தடித்திருக்கும்

அறிகுவாய் சூதகத்தின் வாய்வு காணே(14)

- ✓ Amenorrhoea.
- ✓ Lower abdominal pain.
- ✓ Head ache.
- ✓ Obesity.

(iii) According to the text, Pathinensiddharkal Aruliseidha Naadi Sasthiram

"மாதர்கைபிடித்தபோது வந்திடும்நாடிமூன்றும்

சேதமாயிற்றுநின்று சேரவேபதிந்துநிற்கில்

ஓதுமேசூதகத்தி லோங்கியவாய்வுநின்று

பேதமாய்வாதைபண்ணி பிணிகளைவிளைக்குந்தானே"(15)

If the three Naadis are diminished and found mingled with one another then it indicates vaayu accumulated in uterus.

(iv) According to the text, Agasthiyar Vaithiya Kaaviyam 1500

வானென்ற வித்துபோலே வாயுவும் உருளும்பாரு

ஊனென்ற பசிதான் போகும்

முளைத்ததுதான் இரைச்சல் உண்டாம்

மானென்ற கழிச்சல் மீளும் வரும் சூதகவாயுவாமே(16)

- Loss of appetite.
- Diarrhoea.

These are due to accumulation of vaayu in ovaries.

(v) According to the text, Thirumoolar Karukadai Vaithiyam -600

" சித்தான கர்ப்பத்தில் சேர்ந்திடும் இரத்தந்தான்

வந்தாம் வுருண்டு வாயுபோல் ஓடிடும்

உற்ற பசிபோகும் உழன்றே இரைந்திடும்

வற்றாக் கழிச்சலாம் வன்சூதக வாயுவே"(17)

(vi) According to the text, Brammamuni Vaithiya Soothiram -390

"கண்டுபார் சூதகத்தி லுதிரம் போகா

காலோடு கைமேலும் கடுத்துக் குத்தி

செண்டுபார் வயிற்றிலே தோஷந்தங்கி

திறட்சி குன்மவாயுவொடு சூலை யாச்சு

ஆண்டுபார் சூதகவாயு வாச்சு

அபானமாங் கருக்குழி யிலுதிரங் கட்டி

உண்டுபார் உதிரத்தில் வாய்வு கூடி

உள்ளங்கால் நகக்கண் குதலாச்சே"(18)

- ❖ Amenorrhoea.
- ❖ Body pain.
- ❖ Gastritis.
- ❖ Pricking pain in foot and nail buds.

OTHER TERMS OF KARPA NOIGAL SIMILAR TO SOOTHAGA VAAYU

In Thirumular Karukkadai Vaithiyam 600 described as

"நந்தி உரைத்தது நலமான கர்ப்பத்தில்

அந்நிய நோய்தான் அறுவகை கேளுநீ

புந்தியில் வாயுவும் தேயுவும் கூடிடில்

மந்தி மலடாவாள் மரண வரைக்கென்னே"[19]

In Pathinen Siddhargal Paadiya Vaithiya Sillarai Kovai described as

கருக்குழியின் ஆறுவியாதிகள்

புகலுகிறேன் முதற்றரந்தான் மலடி யென்றப்

பூவைக்குள் கருக்குழிதான் விளக்கமற்று

அகலுகிறேன் அகலாமற் பாசம் பற்றி

அடைந்திருந்தால் விந்தங்கே அணுகா தப்பா

நிகலுகிறேன் மறுதரந்தான் கருக்குழியில்வாயு

நிறைந்திருந்தால் விந்தங்கே நேரா தப்பா

தகலுகிறேன் பின்னுமைங்கு கருக்குழியில் மூடி

தசைவளர்ந்தால் விந்தங்கே தான் செல்லாதே

செல்லாது நாலாவ தப்பா கேளு

சிறியவட் கருக்குழியில் புழுதான் சேரில்

செல்லாது ஐந்தாவ தப்பா கேளு

சொரிந்தங்கே கருக்குழியில் சோரிகட்டி

செல்லாது ஆறாவ தப்பா கேளு

செப்புகிறேன் கருக்குழிதான் மதர்த்தி ருந்தால்

சொல்லாத அவையாறும் வியாதியாகும்(20)

Types of Uterine disorders:

1. Abnormalities in the uterine cavity
2. Endometrial Polyp in the uterus
3. Fibroid uterus
4. Any infection in the uterus
5. Amenorrhoea
6. Bulky uterus

1. KARPA SOOLAI:

கேளாய் பெண்ணே கர்ப்பசூலை கெடுதிசெய்யும்வழிமார்க்கம்

மீளாக் கனலுங் கருக்குழியில் மிகுந்த வாயு வனுசரிக்கும்

நீளாச் சூதகம் தான்புரண்டு நிறைந்த சோரி சிசுபோலாம்

தாளா வயிறு தான்வலிக்கும் தனித்து சேரப் பலன்கெடுமே(21)

-Aaviyalikum Amudhamurai Churrukam

- Pseudopregnancy.
- Abdominal pain.
- Fatigue.

These are the symptoms of karupai soolai due to accumulation of vaayu and agni in ovaries.

2. KARPA VAAYU:

பொருமி ரத்தந்தனை மறித்துப்போத மிகவும் வலியுண்டாங்

குருதிசேரா வயிறுவலிபோங் கொள்ளுங்கர்ப்பந்தனையழிக்கும்

வருடியிடுப்புக் குடைந்துளைக்கும் மலத்தை மிகவும் மிறுக்கிறுக்கி

பெருகப் பணைக்கு மெனப் பெரியோர் பேசுங்கர்ப்பவாயுவிதே(22)

-Dhanwanthri Vaidhiyam Part-1

The symptoms mentioned in the above text due to derangement of vaayu include inhibition of regular menstrual flow, dysmenorrhoea, miscarriage, low back pain, and constipation.

3. KARPA SURONITHAM:

திரண்டு புரண்டு கீல்வயிற்றில் திங்கள் முழுக்கில் வலியுண்டாகும்

மருண்டு குருதி குறுகிவரும் வாய்நீருறு மயங்கிவருந்

திரண்டு சிலநாட் சிக்கிநிற்கும் திறமாங் கருவை யழிப்பிக்கு

முருண்ட கர்ப்பச் சூரோணிதமென் றுரைக்குங் குணங்கண்டறிவீரே(23)

-Dhanwanthri Vaidhiyam Part-2

In Karpa suronitham due to the effect of vaayu in lower abdomen mentioned in the above text it has the symptoms of dysmenorrhoea, oligomenorrhoea, increased salivation, giddiness, irregular menstruation and miscarriage.

4. KARPA VIPURUDHI:

"கூறிடவே கெற்ப்பவிற் புருதிதானும்

குருதிபோல் வயிறினில் சூதகட்டும்

மாறவே தலைவலிக்கும் வீட்டுப்பக்கம்

வயிற்றுவலி யிருதுடையு முளையுமேதான்

சீறவே புழுத்திரண்டு மலமிருக்கும்

சிசுகெர்ப்பந்த் தரியாது வுடலுளைக்கும்

ஆறவே யிக்குணைங்கள் தானறிந்து

அப்பனே மருந்துண்ணச் சித்தியாமே."(24)

-Aathmaratchamirthamenum vaithiya sara sangiragam

- Amenorrhoea
- Headache
- Dysmenorrhoea
- Constipation
- Infertility
- Body pain

5. KARPA VAAYUVIN GUNAM:

"இனிதாகவே சேர்ப்பது வாயுவின் செய்கை

இதமாகவே விள்ளுவேன் கேள்

இனிய மாதவிடாய் காலமது தன்னிலே

வயிறுநோவு அதிகமாக எழுமே

கனிவாக அடிவயிறு கனமாகவே குத்துவலி

நோவு அதிகரிக்கும்

கருதும் இருகொங்கையும் அழலும்

களைக்குமே நெஞ்சுகளையும் அஞ்சலுறவே

நனிவாய் சுரோணிதம் இறைஞ்சிக் கழுநீருபோல்

வாயுமிடை விட்டு ருதுவாம்

நளினமொடு போகமே செய்தால் இறைச்சி நீர்

போலே துகில் மீது காணும்

தனியதி கர்த்திலும் தேகம் வெளுத்திடும்

யோனியதிலூரல் உண்டாம்

தவறாது அன்னம் புகல்வாயில் துவர்ப்பதும்

கண்ணையர் கால் கடுக்கும்".(25)

-Sarabenthirar vaithiya muraigal

- Dysmenorrhea
- Lower abdominal pain
- Pain in the breast
- White discharge

6. SOOTHAGA KIRANI:

"சூதகமாம் போதெல்லாம் வலித்திரத்தம்

வீழ்வதற்கும் சொலு நாக்குட்

பேதகமாய்க் கெடுதப்பி வலிக்கினும்

சூதகக் கிராணி யன்றுபேராம்".

- Dysmenorrhea
- Irregular menstruation

MUKKUTRA IYAL (The Tridosha theory)

Tridosha is otherwise called as mu as they remain as doshas and form as the causative factor for the appearance of disease. This is only a part of the Panchabootha thathuvam and forms the humoral pathology in Siddha system of medicine similar to hormones in modern physiology.

A right understanding of tridosha theory in all its varied aspects is necessary for a rational diagnosis and effective treatment.

“ வாதமாய் படைத்து பித்த வன்னியாய் காத்துச் சேட்ப

சீதமாய் துடைத்துப் பாராந் தேகத்திற்குடியா மைந்து

பூதவிந்தியாமைவர் பூசை கொண்டவர்பால் விந்து

நாதமாங் கிருட்டிண மூர்த்தி நமக் கென்றும் துணையாவாரே”(26)

-Noi Nadal Noi Mudhal Nadal Thirattu (Part-1)

முக்குற்றங்களின் இருப்பிடம்:

“வளிமுதலா யெண்ணிமுக் குற்ற மெல்லாம்

வாழ்வதெனும் தேகமுற்றும் பம்பிப்பர்ந்து

தெளிவுச் சாற்றும் நாபிக் குக்கீழ் வாதம்

தீயிங்கூ றாமழ்லோ உந்திய யாவிக்

கொளிதருசெந் நீரியக்கும் இதயத்திடையில்

உருதிகனம் நெய்ப்பிளக்க ஊட்டும் ஐயம்

நளினத்தின் மேல்தைங்கும் தானமெனவே

நவில்வ ரறி மருத்துவநூல் நல்லூலோர் தமே.”(27)

-Siddha Maruthuvanga Surrukam

The three humours vatha, pitha, kabha are living all over the body. The vatha is distributed below the umblicus, pitha is distributed between the umblical and epigastric region and kabha is distributed above the epigastric region.

Panchaboothams are manifested in the body as three vital forces,

- Vatham (Air + Space)
- Pitham (Fire)
- Kapham (Water + Earth)(28)

S.NO	TRIDOSHAS	SEATS	PROPERTIES	FUNCTIONS
1	**VATHAM**	Below the navel, urinary bladder, intestine, pelvis, umblical cord, thigh, bone, skin, nerve endings, joints, musculature, hair root.	Dryness, lightness, clearness, coolness, mobile formless.	Stimulation, respiration, thinking, sensory functions, coordination of the physical constituents, reflex actions.
2	**PITHAM**	Between the heart and navel, sweat, lymph, blood, stomach, urinary bladder, heart, saliva, eye and skin.	Dry, cold, light, subtle, keen, soft, liquid, bitter.	Body temperature, digestion of food, vision, sweat.
3	**KABHAM**	Above the heart, stomach, fat, sperm, uvula, bone marrow, blood, nose, nerves eyes, joints.	Heavy, cold, sweet, stable and slimy.	It gives strength of joints, shiny appearance of skin, moistens food, cools the eye, softness, firmness.

FUNCTIONS OF VALI:

"ஒழுங்குடன் தாதேழ்மூச் சோங்கி இயங்க

எழுச்சிபெற எப்பணியும் ஆற்ற – எழுந்திரிய

வேகம் புலன்களுக்கு மேவச் சுறுசுறுப்பு

வாகளிக்கும் மாந்தர்க்கு வாயு".(29)

-**Siddha Maruthuvanga Surrukam**

Vatha is said to be first originated from the natural element air and then with the combination of the other two elements, heat and water developed as vatha, and involution of typical type of synthetic chemical changes occur before it is represented in the human body as a humour of vatha dosha. This is classified into ten varieties.

S.NO	TYPES OF VATHAM	FUNCTIONS	IN SOOTHAGAVAAYU
1	Piraanan	It is mainly responsible for respiration and it is necessary for proper digestion and utilisation of food materials.	Normal
2	Abaanan	This is responsible for all downward movements such as passing urine, stools, semen, menstrual flow etc.	Irregular menstruation, Constipation.
3	Viyanan	This is responsible for sense of touch extension and flexion of the part of the body and distribution of the nutrients to various parts of the body.	Low back pain, Lower abdominal pain.

4	Uthaanan	Responsible for all upward visceral movements such as nausea, vomiting etc.	Normal
5	Samaanan	This aids in proper digestionand it controls the other types of vaayu.	Affected
6	Naagan	Helps in opening and closing of the eyelids.	Normal
7	Koorman	Responsible for vision, lacrimation and yawning.	Normal
8	Kirugaran	Induces appetite, salivation, all secretions in the body including nasal secretions and sneezing.	Normal
9	Thevathathan	Induces and stimulates a person to become alert, get anger, to quarrel, to sleep.	Normal
10	Dhananjeyan	Resides in the cranium and produces bloating of the body after death. This leaves from the body after 3days of death, forming a way through the skull.	–

In Soothagavaayu patients Abaanan, Viyanan, Samanan are mainly affected.

PITHAM:

"பசிதாகம் ஓங்கொளிகண் பார்வைபண் டத்து

ருசிதெரி சத்திவெம்மை வீரம் – உசித

மதிகூர்த்த புத்திவனப் பளித்துக் காக்கும்

அதிகாரி யாங்கா னழல்".(30)

-**Siddha Maruthuvanga Surrukam**

Pitha is said to be originated first from the natural element of heat and then with the combination of other two elements viz. air and water, developed as pitha and after the involution of synthetic chemical changes it is represented in the human body as a humour of pitha dosha. This is also sub-divided into five types.

S.NO	TYPES OF PITHAM	FUNCTIONS	IN SOOTHAGAVAAYU
1	Analagam	It promotes appetite and helps in digestion.	Normal
2	Ranjagam	It is responsible for the colour and contents of the blood.	Normal
3	Praasagam	It gives complexion to the skin.	Normal
4	Saathagam	It controls the whole body and is held responsible for fulfilling a purpose.	Lack of regular menstruation.
5	Aalosagam	It is responsible for the perception of vision.	Normal

In Soothagavaayu patients Sathagam is mainly affected.

KABHAM:

"திடமீயு மென்பிணைப்புத் திண்மையுற்ற யாப்பும்

அடலோர் வழுவழுப்பும் ஆக்கைக் – கிடர்க்கு

வெருவாப் பொறுமையும் மேலான காப்பாம்

பெருமைத்தா மையமெனப் பேசு".(31)

-Siddha Maruthuvanga Surrukam

Kabham is said to be originated first from the natural element namely water and then with the combination of other two elements air and heat, it develops as kapha and after the involution of synthetic chemical changes it is represented in the human body as humour in kabha dosha. This kabha dosha is said to possess the destruction power. This is of its coldness which when markedly increased overlaps other two doshas vatha and pitha which are responsible for the respiration, circulation of blood and maintain of head and remains as the signs of life with the result death occur.

S.NO	TYPES OF KABHAM	FUNCTIONS	IN SOOTHAGAVAAYU
1	Avalambagam	Lies in respiratory organ, controls the heart and circulatory system and other types of Kabham.	Normal
2	Kilethagam	Found in stomach, makes the food moist soft and helps to be digested.	Normal
3	Pothagam	Responsible for the sensory Perception of taste.	Normal
4	Tharpagam	Present in the head and responsible for coolness of both eyes, sometimes may be referred to as cerebrospinal fluid.	Normal
5	Santhigam	Necessary for the lubrication and the free movements of the joints.	Low back pain

In Soothagavaayu patients Santhigam is affected.

UDAL THATHUKKAL (SEVEN PHYSICAL CONSTITUENTS):

The human body is made of seven basic physical constituents. These constituents should be in harmony and function normally. Any variation in them will lead to their functional deviations. The Natural characters of the seven physical constituents are mentioned.

S.NO	SAPTHA THATHUKKAL	FUNCTIONS	IN SOOTHAGA VAAYU
1	Saaram	Responsible for the growth and development. It keeps the individual in good temperament and it enriches the blood.	Tiredness
2	Seneer	Responsible for the colour of blood and for the intellect, nourishment, strength, vigour and valour of the body.	Normal
3	Oon	Gives look able contour to the body as needed for the physical activity. It feed the fat next day and gives a sort of plumpness to the body.	Obesity
4	Kozhupu	Lubricates the organs to facilitate frictionless functions.	Normal
5	Enbu	Supports and protects the vital organs, gives the definite structure of the body and responsible for the posture and movements of the body.	Low back pain
6	Moolai	Nourishes the bone marrow and brain which is the centre that controls other systems of body.	Normal

7	Suronitham	It is responsible for the reproduction.	Irregular menstruation

In Soothagavaayu patients Saram, Oon, Enbu, Suronitham are mainly affected.

PINIYARI MURAIMAI (DIAGNOSIS):

It means the method of diagnosing the disease,

“மதித்திடற் கருமை வாய்ந்த

மாண்பரி கார மெல்லாந்

துதித்திட வுணர்ந்தா னேனுந்

துகளறப் பிணியின் றன்மை

பதித்திட வுணரா னாகிற்

பயனுறா னாக லானே

விதித்திடு பிணித்திறத்தை

விளம்புது முதற்கண் மன்னோ”.(32)

-Sikitcharathna Deepam Ennum Vaidhiya Nool

The above poem describes that diagnosis is very important for the physician to treat the disease.

“நோயறிந்து நோய் முதலி நோக்கறிந்து நோவுதன்

தாயறிந்து போக்குந் தாமறிந்து காயநிலை

நொந்தழியா வண்ணகர்விப்பார் நோயினர்க்கு

தந்தையெது நற்பண்டிதர்”.(33)

-Theraiyar Yamaga Venba

Four steps are followed in diagnosing the disease. They are,

1. Poriyaalaridhal
2. Pulanaltherdhal
3. Vinaathal
4. Envagaithervu

1.PORIYAALARIDHAL:

The physician should carefully observe the changes that occur ithe five sensory organs (Porigal) of the patient.

2.PULANALTHERDHAL:

The physician carefully applies his five senses of perception, smell, taste, vision, touch and sound to understand the condition of the patient.

3.VINAATHAL:

The physician should interrogate about the patients name, age, occupation, socio economic status, food habits, history of past illness, history of present illness, family history, marital status, menstrual history and frequency of pain.

ENVAGAI THERVUKAL:

“நாடிப்பரிசம் நாநிறம் மொழிவிழி

மலம் மூத்திரமிவை மருத்துவராயுதம்”(34)

-Noi Nadal Noi Mudhal Nadal Thirattu

Nowadays advanced diagnostic tools have been developed by modern bio-medical scientists. But Siddhars have given eight diagnostic methodological tools. They are called as Envagaithervu.

EIGHT FOLD SYSTEM OF CLINICAL ASSESSMENTS:

Siddhars have given eight diagnostic methodological tools. They are,

1. Naadi
2. Sparisam
3. Naa
4. Niram
5. Mozhi
6. Vizhi
7. Malam
8. Moothiram

NAADI:

"பாரே நாடி அறிந்துணர்ந்து பரமன் செயலும் பிணஈமுறையும்

நீரே ஓடும் சலமும் நிறமுங் குணமும் முகக்குறியும்

காரே யிளகுங் குழல்மடவீர் கால தேக வயதிளமை

நேரே யறியு முகநாடி நெறியும் தெளிவும் சொல்வாமே".(35)

-Sikitcha Rathna Deepam Ennum Vaidhiya Nool

The heart is the special organ of the body. It supplies blood all over the body. Naadi is a Unique pulse reading method to denote any dysfunction of the body.

NAADI MOONDRAIYUM NAADIDUM KAALAI:

"நடுவிரல் நாடியே கணிப்பான்

நற்றவர்க்குருவென நவிலு மறையே

மூன்றிலொன் றுயர்ந்ததை முன்ன றறிந்து

முந்தியதனை யொழித்திடு மருந்திடு

தணியும் நோயின் தந்திரமிதுவே

பேணிக் கணித்திடின் பிறவாய் பின் குணம்".(36)

-Noi Nadal Noi Mudhal Nadal Thirattu

From these stanzas it is very clearly understood that the diagnosis based on Naadi will bring out the best results. Pulse diagnosis is the confirmative diagnosis. Normally the pulse is recorded in a radial artery in the right hand for the male and left hand for the female by keeping the ring finger, the middle finger, and the index finger on it after gently scrubbing the area. It is one unit in vatha as felt by the ring finger, and a half unit in pitha as felt by the middle finger and one fourth unit in kapha as felt by the index finger. The different diseases could easily be diagnosed with the aid of the pulse.

“கரிமுகனடியை வாழ்த்தி கைதனில் நாடி பார்க்கில்

பெருவிரல் குலத்திற் பிடித்தடி நடுவே தொட்டால்

ஒரு விரலோடில் வாதம் உயர் நடுவிரலிற் பித்தந்

திருவிரல் மூன்றிலோடிற் சேத்தும நாடியாமே”.(37)

-Noi Nadal Noi Mudhal Nadal Thirattu

VADHA NAADI:

“வாதமெனும் நாடியது தோன்றில்

சீதமந்தமொடு வயிறு பொருமல் திரட்சி வாய்வு

சீதமுறுங் கிராணி மகோதரம் நீராமை

திரள்வாய்வு சூலை வலிகடுப்புத் தீரை

நீதமுறுங் கிருமிகுன்மம் அண்டவாதம்

நிலையும் நீர்க் கிரிச்சரங்கள் தந்துமேகம்

பேதகமா முதரப்பிணி மூலரோகம்

பேசவெகு பிணிகளுமே பொருள தாமே”.(38)

-Noi Nadal Noi Mudhal Nadal Thirattu

“மாதர் கைபிடித்த போது வந்திடும் வாதநாடி

தீதுறவெடித்து பாய்ந்து சிதறியே சிலம்பினின்றாற்

பேதைதன் வயிற்றின் உள்ளே பெருகு சுரோணிதமே தங்கி

வாதக பண்ண மாதவிடாய்காலம் வருத்தம் செய்யும்

இடுப்போடு கடுத்து நொந்து இடைவிடாக் குத்தலுண்டாய்

தடுத்திடா கர்ப்பந்தன்னை தங்கிடா வண்ணம் செய்யும்”.(39)

-Pathinensiddhargal Aruliseidha Naadi Sasthiram

“மாதர்கைபிடித்த போதுவந்திடும் நாடி மூன்றும்

சேதமாயிற்று நின்றசேரவே பதிந்து நிற்கில்

ஓதுமே சூதகத்தில் ஓங்கிய வாய்வே நின்று

பேதையாய் வாதைபன்னி பிணிகளை விளைவிக்குந்தானே”.(40)

- Pathinensiddhargal Aruliseidha Naadi Sasthiram

VADHA ROGANGAL:

“சொல்லவே வாதமது மீறீற்றானால்

சோர்வடைந்து கைகால்க ளசதியுண்டாம்

மெய்முடங்கும் நிமிரவொண்ணாத் திமிருண்டாகும்

வல்லவே யுடல்பொருமும் வயிறுளைக்கும்

விரும்பி யன்னிஞ் செல்லாது விந்துநஷ்டம்

கொல்லவே நாப்புளிக்குங் கழிச்சலுண்டாம்

கூறினார் மலையமுனி கூறினாரே”.(41)

-Sikitcha Rathna Deepam Ennum Vaidhiya Nool

S.NO	ENVAGAI THERVU	CHARACTER	IN SOOTHAGA VAAYU
1	Naadi	---	Vatha naadi
2	Naa	Coated Taste Colour	Tongue is coated and pale.
3	Niram	Skin colour	Hyperpigmentation in cubital fossa, armpits, neck, thigh, etc [A.Nigricans]
4	Mozhi	Articulation and speech	No abnormality in speech.
5	Vizhi	Niram (pallor, icterus)	Pale in anaemic condition.
6	Sparism	Touch Pain Temperature	No abnormality
7	Malam	Niram – Colour Irugal, Illagal Consistency Manam – Odour	Constipation
8	Mootthiram	Niram – Colour Manam – Smell Nurai – Forth Eadai – Specific gravity Enjal – Deposit	No abnormality

NEERKURI:

"அருந்துமாறிரதமும் அவிரோதமதாய்

அஃகல் அலர்தல் அகாலவூண் தவிர்ந்தழற்

குற்றளவருந்தி உறங்கி வைகறை

ஆடிக்கலசத் தாவியே காதுபெய்

தொருமுகூர்த்தக் கலைக்குட்படு நீரின்

நிறக்குறி நெய்க்குறி நிருமித்தல் கடனே".(42)

-Noi Nadal Noi Mudhal Nadal Thirattu

The early morning urine of the patient is analysed by dropping a drop of gingelly oil on the surface of the urine sample. By dispersing under the sunlight without any external disturbances of the urine sample the accumulation, formations and changes can be noted.

NEIKURI:

"ஐக்குறி கொடுவட வானிழ லமாந்தோர்

கைக்குறி தெரித்த நங்கடவுளைத் துதித்தே

மெய்க்குறி நிறந்தொணி விழிநா இருமயம்

கைக்குறி முழுவதூவங் கற்றார் தம்மினும்

பொய்க்குறி மெய்க்குறி புகலுமெவர்க்கு

நெய்குறியதனை இந்நீனியத் துரைப்பாம்".(43)

-Noi Nadal Noi Mudhal Nadal Thirattu

The urine is kept on the kidney tray in sunlight, on a non-windy condition. Then it should be examined by dropping a drop of gingelly oil gently, with a stick. If the oil spreads like a snake it indicates Vatha, a ring indicates Pitha, and if it floats like a pearl it indicates Kapha.

“அரவென நீண்டினஃதே வாதம்

ஆழி போற் பரவின் அஃதே பித்தம்

முத்தொத்து நிற்கின் மொழிவதென் கபமே”.(44)

-Siddha Maruthuvanga Surrukam

In Soothagavaayu when a drop of oil is put in the patient’s freshly collected urine the oil drop spread like a snake which indicates vatha neer.

The eight tools of diagnosis are used not only for that purpose, but also to study the prognosis. The urine examination is widely used to study the prognosis. If the oil drop for the urine examination spreads in the shape of rice pot, a dwarf, betel leaf, horse, the prognosis is good. But if it spreads like a bird, dog, lion, pig, monkey, scorpion, cat, human being, the prognosis is bad. If the drop spreads rapidly the prognosis is bad. If the drop spreads slowly the prognosis is good and the disease is easily curable.

LINE OF TREATMENT:

Administration of the trial medicine:

Kalingathi Ennai-15ml with warm water**,** once a day before food.

Duration of treatment:

5days, three consecutive menstrual cycles.

Yogasanam:

All patients were advised to do yogasanam. Yoga is a part of Siddha medicine which plays a major role in not only treating the disease but also in preventing the disease. Women should keep in mind that they should not do asanas during their monthly menstrual cycle. After, the period ends, asanas can be practised and it will give a lot of benefits(45).(Fig 1.1-1.5).

- Piranayamam
- Dhanurasanam
- Bujangasanam
- Badhakonasanam
- Patchimothasanam

Fig 1.1 Pranayamam

Fig 1.2 Bujangasanam

Fig 1.3 Dhanurasanam

Fig 1.4 Badhakonasanam

Fig 1.5 Patchimothasanam

MODERN ASPECT

MODERN ASPECT

FEMALE REPRODUCTIVE SYSTEM:

The female reproductive system consists of external and internal genitalia organs respectively.

EXTERNAL GENITALIA:

The external female genitalia are referred to as vulva. It consists of the following structures namely,

1 .MONS PUBIS
2. LABIA MAJORA
3. LABIA MINORA
4. CLITORIS
5. OPENING OF THE URETHRA (MEATUS)
6. HYMEN
7. PERINEUM

The vestibule is the space into which the vagina and urethra open. The urethra opens just anterior to the vagina.

The vestibule is bordered by a pair of thin, longitudinal skin folds called the labia minora.

Lateral to the labia minora two prominent rounded folds of skin called the labia majora are present. The two labia majora unite anteriorly into an elevation of tissue over the pubic symphysis called the mons pubis. The lateral surface of the labia majora and the surface of the mons pubis are covered with coarse hair.

The medial surface of the labia majora are covered with numerous sebaceous and sweat glands. The space between the labia majora is called the pudendal cleft.

A small erectile structure is called the clitoris is located in the anterior margin of the vestibule. The two labia minora unite over the clitoris to form a fold of skin called the prepuce.

The hymen is a thin fold of mucous membrane that separates the lumen of the vagina from the urethral sinus.

The perineum is the short stretch of skin starting at the bottom of the vulva and extending to the anus.

INTERNAL GENITALIA:

The internal reproductive organs are situated in the pelvis between the bladder and rectum. They are held in space within the pelvis by a group of ligaments.

The internal genitalia includes

1. VAGINA
2. CERVIX
3. UTERUS
4. FALLOPIAN TUBES
5. OVARIES

VAGINA:

- The vagina is a muscular, hollow tube that extends from the vaginal opening to the cervix of the uterus. It is also known as the birth canal.
- It is a fibro muscular tube of about 10cm long.
- It is a female organ of copulation and allows menstrual flow and child birth. In young females it is covered by a thin mucous membrane called hymen.

CERVIX:

- The cervix is the lower, narrow portion of the uterus where it joins with the top end of the vagina.
- During menstruation, the cervix stretches open slightly to allow the endometrium to be shed.
- During childbirth, contractions of the uterus will dilate the cervix up to 10cm in diameter to allow the child to pass through.

UTERUS:

- The uterus is a hollow, pear-shaped organ which is divided into parts namely cervix, which is the lower part that opens into the vagina, and the main body of the uterus, called the corpus.
- The uterine wall is composed of three layers,
- Outer serous layer or perimetrium,
- Middle muscular layer or myometrium,
- Inner most layer endometrium.
- The endometrium consist of simple columnar epithelial cells with underlying connective tissue layer. The superficial part of endometrium is sloughed down during menstruation.

FALLOPIAN TUBES:

- There are two uterine tubes also called uterine tubes or oviducts.
- One uterine tube is associated with each ovary.
- The uterine tubes extend from the ovaries to the uterus.
- They open pear the ovary to receive the oocyte and the opening is surrounded by long thin processes called fimbriae.
- As soon as oocyte is ovulated, it comes into contact with the surface of the fimbriae and the cilia on the fimbrial surface sweep the oocyte into the uterine tube.
- Fertilization usually occurs in the uterine tube near the ovary.

OVARIES:

- The two ovaries are small oval shaped organs attached to the ligaments that suspend them in the pelvic cavity and from the ligament of the uterus.
- The suspensory ligament extends from each ovary to the lateral body wall and the ovarian ligament attaches the ovary to the uterus.
- A layer of visceral peritoneum called tunica albuginea covers the ovary. The outer cortex of the ovary is made up of dense connective tissue containing ovarian follicles. Each of the ovarian follicles contains an oocyte the female germ cell.[46],[47]

PHYSIOLOGY OF MENSTRUAL CYCLE

DEFINITION:

- The term menstrual cycle refers to the series of changes that occur in sexually mature non pregnant females and that culminate in menses.
- The term menses is derived from Latin word which means month. Menses is a period of mild haemorrhage during which part of the endometrium is sloughed and expelled off from the uterus.
- The commencement of menstrual cycle is called menarche and usually starts at the age of 12-15 years.
- Permanent cessation of menstrual cycle in old age is called menopause and it usually occurs at the age of 45-50 years.

DURATION OF MENSTRUAL CYCLE:

The menstrual cycle is about 28 days long and the changes are controlled by the secretions of FSH and LH from the anterior pituitary.

SYMPTOMS OF MENSTRUAL CYCLE:

- Acne
- Feeling tired
- Trouble sleeping
- Swollen or tender breasts
- Upset stomach, bloating, constipation or diarrhoea
- Headache or backache
- Appetite changes or food cravings
- Joint or muscle pain
- Trouble with concentration or memory
- Tension, irritability, mood swings or crying spells
- Anxiety or depression.

Symptoms vary from woman to woman.

PHASES OF MENSTRUAL CYCLE

The day count for menstrual cycle begins on the first day of menstruation when blood starts to come out of the vagina. In this section, the length of menstrual cycle has been assumed to be 28 days (which is the average among women). The entire duration of a menstrual cycle can be divided into four main phases:

- Menstrual phase (From day 1 to 5)
- Follicular phase (From day 1 to 13)
- Ovulation phase (Day 14)
- Luteal phase (From day 15 to 28)

MENSTRUAL PHASE (DAY 1-5):

Menstrual phase begins on the first day of menstruation and lasts till the 5^{th} day of the menstrual cycle. The following events occur during this phase:

- The uterus sheds its inner lining of soft tissue and blood vessels which exits the body from vagina in the form of menstrual fluid.
- Blood loss of 10 ml to 80 ml is considered as normal.
- Abdominal cramps may occur. These cramps are caused by the contraction of the uterine and the abdominal muscles to expel the menstrual fluid.

FOLLICULAR PHASE (DAY 1-13):

This phase also begins on the first day of menstruation, but it lasts till the 13^{th} day of the menstrual cycle. The following events occur during this phase:

- The pituitary gland secretes a hormone that stimulates the egg cells in the ovaries to grow.
- One of these egg cells begins to mature in a sac like structure called follicle. It takes 13 days for the egg cell to reach maturity.
- While the egg cell matures, its follicle secretes a hormone that stimulates the uterus to develop a lining of blood vessels and soft tissue called endometrium.[48]

OVULATION PHASE (DAY 14):

On the 14th day of the cycle, the pituitary gland secretes a hormone that causes the ovary to release the matured egg cell. The released egg cell is swept into the fallopian tube by the cilia of the fimbriae. Fimbriae are finger like projections located at the end of the fallopian tube close to the ovaries and cilia are slender hair like projections on each Fimbria.

LUTEAL PHASE (DAY 15-28):

This phase begins on the 15 th day and lasts till the end of the cycle. The following events occur during this phase:

- The egg cell released during the ovulation phase stays in the fallopian tube for 24 hours.
- If a sperm cell does not impregnate the egg cell within that time, the egg cell disintegrates.
- The hormone that causes the uterus to retain its endometrium gets used up by the end of the menstrual cycle. This causes the menstrual phase of the next cycle to begin[(49)].

MENSTRUAL CYCLE:

The term menstrual cycle refers to the series of changes that occur in sexually mature non pregnant females and that culminate in menses.

The term menses is derived from Latin word which means month. Menses is a period of mild haemorrhage during which part of the endometrium is sloughed and expelled off from the uterus.

The menstrual cycle is about 28 days long and the changes are controlled by the secretions of FSH and LH from the anterior pituitary.

The ovarian cycle and the endometrial cycle together constitute menstrual cycle.

OVARIAN CYCLE:

The development and maturation of a follicle, ovulation and formation of corpus luteum and its degeneration constitute an ovarian cycle. All these events occur within 4 weeks. Ovarian cycle consists of Recruitment of groups of follicles, Selection of dominant follicle and its maturation, Ovulation, Corpus luteum formation, Demise of corpus luteum.

RECRUITMENT OF GROUPS OF FOLLICLES (PREANTRAL PHASE):

About 20 antral follicles proceed to develop in each cycle. The growth and differentiation of primordial follicles are under the control ofFSH. Unless the follicles are rescued by FSH at this stage, they undergo atresia. Oocyte is enlarged to the size of a follicle. Oocyte is surrounded by acellular barrier of glycoprotein cells called Zonapellucida.

Flattened outer single layered pregranulosa cells become multilayeredgranulosa cells. Nutrition to the oocyte is maintained through the gap junctions between granulosa cells and oocyte.

In selection of a dominant follicle the development of antrum containing secondary or vesicular follicle from the solid primary follicle depends on FSH. Follicular fluid is produced within theca internae. The fluid filled spaces coalesce to form an antrum. At day 5-7, one of the follicle becomes dominant and undergoes further maturation. Follicle with highest antral concentration of oestrogen and lowest androgen: oestrogen ratio and whose granulosa cells contain the maximum receptors for FSH, becomes the dominant follicle. The rest of them become atretic by day eight. There is marked enlargement of the granulosa cells with lipid inclusion. The cells adjacent to the ovum are arranged radially and are called corona radiate. The fully mature Graffian follicle just prior to ovulation measures about 20mm and is composed of Theca externa, Theca interna, Membranagranulosa, Granulosa cell layer, Discus proligerus and Antrum containing vesicular fluid[(50)].

OVULATION:

The dominant follicle, shortly before ovulation reaches the surface of the ovary. The oocyte completes the first meiotic division. The follicular wall near the ovarian surface becomes thinner. Stigma develops as conical projection and penetrates the outer surface layer of ovary. Stigma is soon closed by a plug of plasma.

CAUSES:

1. Endocrinal - LH surge - FSH rise
2. Stretching factor
3. Contraction of the micromuscles

Menstruation is unrelated to ovulation and anovular menstruation is quite common during adolescence, following childbirth and in women approaching menopause[51].

CORPUS LUTEUM:

After ovulation, the ruptured Graffian follicle develops into corpus luteum. The life cycle is divided into four stages.

1. Proliferation
2. Vascularisation
3. Maturation
4. Regression

ENDOMETRIAL CYCLE:

The endometrium is the lining epithelium of the uterine cavity. It consists of surface epithelium, glands, stroma and blood vessels. Two distinct divisions are seen. They are

1. Basal zone (stratum basalis)
2. Superficial functional zone (stratum functionalis)

BASAL ZONE:

This zone is about one third of the total depth of the endometrium and lies in contact with the myometrium. The zone is uninfluenced by hormone and no cyclic changes are observed.

After shedding of the superficial part during menstruation, the regeneration occurs from this zone. It is about 1mm in thickness.

FUNCTIONAL ZONE:

This zone is under the influence of ovarian hormones, oestrogen and progesterone. The changes during anovulatory cycle can be divided into 4 stages

1. Stage of Regeneration
2. Stage of Proliferation
3. Stage of Secretion
4. Stage of Menstruation

(i) STAGE OF REGENERATION:

Regeneration of the endometrium starts before the menstruation ceases and is completed 2-3 days after menstruation.

(ii) STAGE OF PROLIFERATION:

It extends from 5th day to 14th day until ovulation. During this stage the level of ovarian oestrogen is raised. In these stage blood vessels, glands and other components undergo proliferation.

(iii) STAGE OF SECRETION:

The changes of components are due to the combined effect of oestrogen and progesterone. The progesterone act on the endometrium. It starts on day 15 and ceases 5-6 days prior to menstruation. Thickness of endometrium reaches its highest 5-6mm.

(iv) STAGE OF MENSTRUATION:

Due to damage of blood vessels bleeding occurs. The blood along with the superficial functional layer is shed into the uterine cavity. A normal menstrual cycle depends on cyclical ovarian steroid secretions which in turn are controlled by the pituitary and the hypothalamus and to some extent by the thyroid and adrenal glands. So the hypothalamo-pituitary-ovarian axis is important[(52)].

HORMONAL INTERACTIONS IN THE REPRODUCTIVE FUNCTIONS:

Neuroendocrinology with vast hormonal interactions is responsible for menstrual cycle and reproductive functions in women. A normal menstrual cycle depends on cyclical ovarian steroid secretions which in turn are controlled by the pituitary and the hypothalamus and to same extend by the thyroid and adrenal glands. It is therefore essential to understand the hypothalamic-pituitary-ovarian axis in normal women.

The following hormones play the major role,

1. Gonadotropin releasing hormone (GnRH)- hypothalamus
2. Follicle stimulating hormone (FSH)- anterior pituitary
3. Luteinising hormone (LH)- anterior pituitary
4. Oestrogen- ovary
5. Progesterone- ovary
6. Inhibin- ovary
7. Testosterone- ovary

1.GONADOTROPIN RELEASING HORMONE (GnRH):

- GnRH is secreted by the hypothalamus which modulates the neural control of FSH and LH by the anterior pituitary.
- GnRH is released in a pulsatile manner and the pulsatility and amplitude of its release varies with various phases of the menstrual cycle.
- In pre-ovulatory phase it pulses every 60mins but slows down in luteal phase to one in 3 hours. GnRH is continuous in males but pulsatile in females.
- The hypothalamus is controlled by higher cortical centres especially temporal lobe. Emotional upsets stimulate or depress the H-P-O axis and disturb the menstrual cycle.

2. FOLLICLE STIMULATING HORMONE(FSH):

- FSH controls the ripening of the primordial follicles and in combination with the luteinizing hormone activates the secretion of oestrogen.
- Its activity starts as menstruation is ceasing, it reaches the peak by 7^{th} day and then declines to disappear around 18^{th} day. Another small peak occurs in premenstrual phase.
- Low FSH causes defective folliculogenesis and short or defective corpus luteal phase.

3.LUTEINIZING HORMONE:

- In combination with FSH it activates the secretion of oestrogen, brings about maturation of the ovum and causes ovulation.
- LH stimulates the completion of the reduction division of the oocyte. Following ovulation, it produces luteinisation of the granulosa and the theca cells and initiates progesterone secretion. The LH surge precedes ovulation by 24 to 36 hours.
- The hypothalamus is controlled by higher cortical centres especially temporal lobe. Emotional upsets stimulate or depress the H-P-O axis and disturb the menstrual cycle[(53)].

4.OESTROGEN:

- The main sources of oestrogen are the theca and granulosa cells of the graffian follicles and corpus luteum, while the adrenal cortex is the secondary source.
- Its level increase 6 to 7 days before ovulation and reaches the peak 2 days before ovulation and then declines.
- It increases uterine vascularityand regenerate the endometrium after menstruation and is responsible for the proliferative hyperplasia of the endometrium.

5.PROGESTERONE:

- The corpus luteum is the main source of progesterone. The level rises after ovulation and reaches peak at mid luteal phase. With the degeneration of the corpus luteum, its level falls and brings about menstruation.
- In an anovulatory cycle, progesterone is absent or present in negligible amount and the menstruation is brought by the fall in oestrogen level.
- If pregnancy occurs the corpus luteum continues to enlarge and secrete progesterone. The high level of the hormone prevents menstruation and leads to amenorrhoea of pregnancy[(54)].

6.INHIBIN:

- Inhibin is a peptide secreted by the graffian follicle and suppress pituitary FSH. In normal folliculogenesis FSH and LH initiate the secretion of oestrogen by the graffian follicles. Oestrogen is responsible for the secretion of inhibin in the graffian follicles, which in turn suppress FSH but stimulates LH.
- In polycystic ovarian disease, there is increased secretion of inhibin. This causes a low FSH and LH secretion by pituitary resulting in anovulation.

7.TESTOSTERONE:

- The ovarian stromal cells secrete androgenic products, namely Testosterone, Dihydroepiandrosterone (DHEA) and Androstenedione.
- Androstenedione gets converted to oestrogen in the peripheral fat. The increase in ovarian stroma is responsible for the rise in these hormones and development of hirsutism[(55)].

POLY CYSTIC OVARIAN SYNDROME

HISTORY:

- In 1935 – Stein &Leventhal first described poly cystic ovarian syndrome.
- In late 1960 and early 1970 deranged hypothalamic-pituitary axis is described.
- In 1980 late complications related to insulin resistance.
- By 1980 the use of ultrasound scans, the characterised polycystic appearance was recognized.

PREVALENCE:

- 75% of hirsute women with normal menses but anovulatory cycles.
- 40% of hirsute women with normal ovulatory cycles(mildform of PCOS).
- 20% of normal women have mild form of PCOS.
- 4-7% of female in reproductive age has clinically evident PCOS.
- The prevalence of PCOS depends on the choice of diagnostic criteria. The World Health Organisation estimates that it affects 116 million women worldwide as of 2010 (3.4% of the people).
- One community based prevalence study using the Rotterdam criteria found that about 18% of women had PCOS and that 70% of them were previously undiagnosed.

NOMENCLATURE:

- Poly cystic ovary disease
- Stein- Leventhal syndrome
- Functional ovarian hyperandrogenism
- Ovarian hyperthecosis
- Sclero cystic ovary syndrome

DEFINITION:

Thetwo definitions commonly used are,

Definition 1: (1990) if a female patient has all the following,

- Oligomenorrhoea
- Signs of androgen excess
- Other entities causing poly cystic ovaries are excluded

Definition 2 :(2003) **Rotterdam** indicated pcos to be present if 2 out of 3 criteria are met

- Oligomenorrhoea
- Anovulation
- Poly cystic ovaries (ultra sound)
- Hyperandrogenism[56]

(2006) Rotterdam criteria: A women must have the two of the following three manifestations:

- Excess androgen activity
- Anovulation
- Polycystic ovaries
- Exclusion of other entities

While there are a number of definitions of PCOS, the Rotterdam consensus is the most widely accepted. The Rotterdam criteria require the presence of two of the following:

- Oligo/ Anovulation
- Hyperandrogenism- clinical or biochemical
- Polycystic ovaries on ultrasound[57]

AETIO PATHOGENESIS:

There is disagreement and uncertainty as to what causes polycystic ovarian disease. Poly cystic ovaries and polycystic ovary syndrome have been associated with one or more of these factors:

- Genetic predisposition
- Insulin resistance or hyperinsulinism (high blood levels of insulin)
- Obesity
- Hyperandrogenism (excessive production of male hormones)
- Abnormality of the hypothalamic-pituitary-gonadal axis (organ / hormonal disorder)
- Environmental chemical pollution (hormonal disruptors)
- Food adulteration (excitatory amino acids, for example)
- Chronic inflammation

Some of these causal factors may also be consequences of polycystic ovary disease. In other words, we have an amazingly complex network of interacting variables, each of which influences the other. Polycystic ovarian syndrome is not a simple disease with a single cause.

PATHOGENISIS:

Exact pathophysiology of PCOS is not clearly understood. It may be discussed under the following

- Over secretion of LHRH in hypothalamus causes increased secretion of the LH by the pituitary gland. The LH stimulates the ovarian stroma to secrete androstenodione which is converted to estrone in the fatty tissue.
- The excess of estrone suppresses the secretion of FSH and sensitizes the pituitary to LHRH, increasing the secretion of LH.
- I nhibin F – a poly peptide secreted by the granulosa cells in the ovaries may reduce further the secretion of FSH.
- The increase in the ratio of LH and FSH in the plasma is the characteristic feature of pcod. The imbalances between the LH & FSH become self perpetuating.
- Androstenedione is also converted to testosterone but the concentration of testosterone in the plasma usually remains high in normal range.

- The secretion of oestrogen by ovaries is reduced.
- Obesity is common in the patients with the endocrine imbalance because the adipose tissue possesses aromatase enzyme that converts androstenedione to estrone and testosterone to etradiol.
- Excess of adipose tissue creates both excess androgens (responsible for hirsutism and virilisation) and excess oestrogen (inhibits FSH by negative feedback).
- Hyper insulinaemia increase GnRH pulse frequency, LH over FSH dominance and increased ovarian androgen production. The elevated insulin levels also act on liver to inhibit production of sex hormone binding (SHBH) which leads to an increase in free testosterone.
- Insulin resistance is a common finding among patients of normal weight as well as those overweight patients.
- Insulin like growth factor 1 binding protein is reduced which leads to increased circulating insulin like growth factor 1 enhancing ovarian androgen production.
- Some women may also have increased adrenal androgenic production.
- All these leads to the decreased follicular maturation and anovulation which is the most common cause of infertility[58].

SIGNS AND SYMPTOMS:

Some combination of the following symptoms that vary with each individual:

- Multiple ovarian cysts
- Irregular or absent menses
- Infertility
- Acne
- Obesity or inability to lose weight
- Excessive body or facial hair (hirsutism)
- Insulin resistance and possibly diabetes
- Thinning of scalp hair
- Velvety, hyperpigmented skin folds (acanthosisnigricans)
- High blood pressure
- Polycystic ovaries that is 2-5 times larger than healthy ovaries
- Sleep apnea

- Disordered immune system
- Mood disorders, including anxiety and depression
- Appetite disorder
- High blood fats (cholesterol and triglycerides)
- Increased probability of cardiovascular disease or diabetes
- Multiple hormone imbalances, commonly including:
- Androgens (testosterone)
- Oestrogen
- Progesterone
- Prolactin
- FSH (follicle stimulating hormone)
- LH (luteinizing hormone)
- Cortisol
- Insulin
- Thyroid hormone

COMPLICATIONS:

Women with PCOS are at risk for the following,

- **Endometrial hyperplasia and endometrial carcinoma**

Possibly due to over accumulation of the uterine lining and also lack of progesterone resulting in prolonged stimulation of uterine cells by oestrogen and also may be due to obesity, hyperinsulinaemia and hyper androgenism.

- **Hyper Insulinaemia**

High fasting and post prandial insulin level Peripheral insulin resistance.

- **Type 2 diabetes mellitus**
- **Dyslipidaemia**

Disorder of lipid metabolism, cholesterol and triglycerides. PCOS patients show decreased removal of atherosclerosis inducing remnants.

- **Cerebro and cardio vascular diseases**

Hypertension

Endothelial dysfunction and impaired fibrinolysis (Circulating plasminogen activating factors level) associated with the risk for vascular lesions like ischaemic heart disease and stroke.

- **Infertility**

The chronic elevation of insulin levels and enhanced ovarian sensitivity to insulin combined with elevated LH concentration results in ovarian thecal hyperplasia, increased androgen secretion, arrested follicular development and anovulation resulting in menstrual disturbance and infertility.

- **Miscarriage**

This may be due to lack of progesterone.

- **Acanthosisnigricans**

Patches of darkened skin under the arms, in the groin area and on the back of the neck.

- **Auto immune thyroiditis**

DIAGNOSIS:

The diagnosis is made using the Rotterdam criteria, even when the syndrome is associated with a wide range of symptoms.

STANDARD DIAGNOSTIC ASSESSMENTS:

HISTORY TAKING:

- Specifically for menstrual pattern, obesity, hirsutism and absence of breast discharge.
- These four questions can diagnosis PCOS with a sensitivity of 77.1% and specificity of 93.8%.

GYNAECOLOGICAL ULTRASONOGRAPHY:

- Looking for peripherally placed small ovarian follicles of size 5-7 mm giving the appearance of string of pearls and increased size of the ovaries that is 1.5 to 3 times larger than the normal.

LAPROSCOPIC EXAMINATION:

- This reveals a thickened smooth pearl white outer surface of the ovary.

COMMON ASSESSMENT FOR ASSOCIATED CONDITIONS OR RISKS:

- Fasting blood glucose and lipid profile.
- 2 hour oral glucose tolerance test (GTT) in patients with risk factor (obesity , family history, H/O gestational diabetes) and may indicate impaired GTT in 15% - 30% women with PCOS.
- Frank diabetes can be seen in 65% - 68% of women with this condition.
- Insulin resistance can be observed in both normal weight and overweight patients.
- Fasting insulin level to predict the response to medication.

THE EXCLUSION OF OTHER DISORDERS:

- Prolactin to rule out hyper prolactinaemia.
- TSH to rule out Hypothyroidism.
- 17-hydroxy progesterone to rule out congenital Adrenal hyperplasia.

DIFFERENTIAL DIAGNOSIS:

Other causes of irregular or absent menstruation and hirsutism are,

- Adrenal hyperplasia
- Cushing's syndrome
- Hyper prolactinemia
- Androgen secreting neoplasms
- Other pituitary and adrenal disorder
- Other insulin resistant situations such as acromegaly[59][60].

TRIAL MEDICINE

LITERATURE REVIEW OF TRIAL MEDICINE

KALINGATHI ENNAI

Reference: Sikitcharatna Deepam Irandam Pagamagiya Vaithiya Chinthamani

Ingredients

- Varithumatikai saru (*Citrullus colcocynthis)*
- Vengaya saru (*Allium cepa)*
- Elumitcham palasaru (*Citrus limon)*
- Chitramanakku ennai (*Castor oil)*
- Inji rasam (*Zingiber officinale)*
- Seeragam (*Cuminum cyminum)*
- Dhaniya (*Coriandrum sativum)*
- Sathakuppai (*Anethum graveolens)*
- Lavangam (*Syzygium aromaticum)*
- Lavangapattai (*Cinnamomum verum)*
- Manjal (*Curcuma longa)*
- Elam (*Elettaria cardamomum)*

Standard Operating Procedure

Source of raw drugs:

The required raw drugs are procured from a well reputed indigenous raw drug shop.

Purification of Siddha Drugs:

Siddha drugs are purified as mentioned in Sikitcha ratna deepam ennum vaidhiya nool.

Preparation:

The above mentioned juices and oil are mixed together in a mud pot and boiled. During boiling the above given purified herbal ingredients are made into powder form and mixed together. Finally, oil prepared in the way as mentioned in the literature is safely kept.

Drug Storage:

The trial medicine is stored in a clean air tight dry container and it is dispensed medicament in a labeled container.

Dosage:

15ml once a day

Adjuvant:

Warm water

Duration:

Five days, Three consecutive menstrual cycles[61].

PROPERTIES OF TRIAL MEDICINE:

1.VARITHUMATIKAI (fig 2.1)

Synonyms : Aatruthumati, Kalingam

Botanical name : Citrullus colcocynthis

Suvai : Kaippu

Thanmai : Veppam

Pirivu : Kaarppu

Action : Alterative

Hydragogue

Gastrointestinal irritant

Emetic

General characters :

கிடையெங்கே சோம்பலெங்கே கேடுறச்செய் வாதக்

கடையெங்கே யாற்றுக் கலிங்க- மடைதிறக்கின்

அண்டை யடைச்சலெங்கே யாயிழையார் சூதகத்தின்

உண்டை யுடைச்சலெங்கே யோது[62].

2.VENGAYAM (fig 2.2)

Synonyms : Erulli, Pallandu

Botanical name : Allium cepa

Suvai **:** Kaippu

Thanmai **:** Veppam

Pirivu **:** Kaarppu

Action **:** Emmenagogue

Demulcent

Stimulant

General characters:

வெப்புமூ லங்கிரந்தி வீறுரத்த பித்தமுடன்

செப்புநா அக்கரந்தீ ராத்தாகம்-வெப்புக்

கடுப்பறுமந் தஞ்சந்நி காசம்வயிற் றுப்பல்

தடிப்பேறும் வெங்காயத்தால்[63].

3.ELUMITCHAI (fig 2.3)

Synonyms **:** Sambeeram

Botanical name : Citrus limon

Suvai **:** Pulippu

Thanmai **:** Veppam

Pirivu : Kaarppu

Action : Refrigerant

General charactres:

தாகம் குநகநோய் தாழாச் சிலிபதநோய்

வேகங்கொள் உன்மாதம் வீறுபித்தம்-மாகண்ணோய்

கன்னனோய் வாந்தியும்போங் கட்டுவா தித்தொழிலில்

மன்னெலுமிச் சங்கனியை வாழ்த்து[64].

4.CHITRAMANAKKU (fig 2.4)

Synonyms : Yerandam,Chithiram

Botanical name : Ricinus communis

Suvai **:** Kaippu

Thanmai : Veppam

Pirivu : Kaarppu

Action **:** Anti-vata

Galactagogue

Laxative

General characters :

ஆமணக்கு நெய்யால் நலமுண்டாம் யாவர்க்கும்

பூமணக்கு மேனி புரிகுழலே-வாய்மணக்குக்

கொள்ளில் வயிறுவிடுங் கோரமுள்ள வாயுவறும்

உள்ளில்வரு குன்மம்போ மோது[65].

5. INJI (fig 2.5)

Synonyms **:** Allam, Arthragam

Botanical name **:** Zingiber officinale

Suvai **:** Kaarppu

Thanmai : Veppam

Pirivu **:** Kaarppu

Action : Stimulant

Carminative

Stomachic

Digestive

General characters :

இஞ்சிக் கிழங்குக் கிருமல்ஐயம் ஒக்காளம்

வஞ்சிக்குஞ் சன்னிசுரம் வன்பேதி-விஞ்சுகின்ற

சூலையறும் வாதம்போந் தூண்டாத தீபனமாம்

வேலையுறுங் கண்ணாய் – விளம்பு[66].

6.SEERAGAM (fig 2.6)

Synonyms **:** Asai, Bosanakudari

Botanical name : Cuminum cyminum

Suvai **:** Kaarppu, Inippu

Thanmai **:** Thatpam

Pirivu **:** Inippu

Action : Carminative

Stimulant

Astringent

Stomachic

General characters:

வாயுவொடு நாசிநோய் வன்பித்தஞ் சேராது

காயம் நெகிழாது கண்குளிருந் – தூயமலர்க்

காரளகப் பெண்மயிலே ! கைகண்ட தித்தனையுஞ்

சீரகத்தை நீதினமுந் தின்[67].

7. DHANIYA (fig 2.7)

Synonyms : Kothumalli, Urularisi

Botanical name : Coriandrum sativum

Suvai **:** Kaarppu

Thanmai **:** Seedhaveppam

Pirivu : Kaarppu

Action : Carminative

Stomachic

Stimulant

General characters:

கொத்துமல்லி வெப்பம் குளிர்காய்ச்சல் பித்தமந்தஞ்

சர்த்திவிக்கல் தாகமொடு தாதுநட்டம்-கத்தியெழும்

வாத விகார்மடர் வன்கர்த்த பிவிரணம்

பூதலத்தில் லாதகற்றும் போற்று[68].

8.SATHAKUPPAI (fig 2.8)

Synonyms **:** Madhurigai

Botanical name : Anethum graveolens

Suvai **:** Inippu

Thanmai **:** Veppam

Pirivu : Kaarppu

Action **:** Emmenagogue

Stimulant

Stomachic

Carminative

Antispasmodic

General characters :

வாதமொடு சூதிகா வாதம் சிரசுநோய்

மோதுசெவி நோய்கபநோய் மூடுசுரம்-ஓதுகின்ற

மூலக் கடுப்பு முதிர்பினசம் போகும்

ஞாலச் சதகுப்பை நாடு[69].

9.LAVANGAM (fig 2.9)

Synonyms : Anjugam, Urkadam

Botanical name : Syzygium aromaticum

Suvai : Kaaramum viruvirupumulathu

Thanmai : Veppam

Pirivu **:** Kaarppu

Action **:** Carminative

Antispasmodic

Stomachic

General characters:

பித்த மயக்கம் பேதியொடு வாந்தியும்போம்

சுத்தவிரத் தக்கடுப்புந் தோன்றுமோ-மெத்த

இலவங்கங் கொண்டவருக் கேற் சுகமாகும்

மலமங்கே கட்டுமென வாழ்த்து.

சுக்கிலநட் டங்கர்ண சூர்வியங்க லாஞ்சனந்தாட்

சிக்கல்விடாச் சர்வா சியப்பிணியு-மக்கிக்குட்

டங்கப் பூவோடு தரிபடருந் தோன்றிலில்

வங்கப்பூ வோடுரைத்து வா[70].

10.LAVANGAPATTAI (fig 2.10)

Synonyms **:** Karuvapattai

Botanical name : Cinnamomum verum

Suvai **:** Kaaramum inippum

Thanmai : Thatpham

Pirivu **:** Inippu

Action **:** Stimulant

Carminative

Aphrodisiac

General characters:

தாதுநட்டம் பேதி சருவவிஷம் ஆகியநோய்

பூதகிர கஞ்சிலந்திப் பூச்சிவிடஞ்-சாதிவிடம்

ஆட்டுமிரைப் போடிருமல் ஆகியநோய்க் கூட்டமற

ஓட்டுமில வங்கத் துரி.

சன்னலவங் கப்பட்டை தான்குளிர்ச்சி யுண்டாக்கும்

இன்னுமிரத் தக்கடுப்பை யீர்க்குங்காண்-முன்னமுறும்

உந்திக் கடுப்பகற்றும் உண்மூலப் புண் போக்கும்

கந்தமிகு பூங்குழலே! காண்(71).

11.MANJAL (fig 2.11)

Synonyms : Arisinam, Nisi

Botanical name : Curcuma longa

Suvai : Kaarppu, Kaippu

Thanmai : Veppam

Pirivu **:** Kaarppu

Action : Carminative

Stimulant

General characters:

பொன்னிறமாம் மேனி புலனாற்ற மும்போகும்

மன்னு புருட வசியமாம்-பின்னியெழும்

வாந்திபித்த தோடமையம் வாதம்போந் தீபனமாங்

கூர்ந்தமஞ்ச ளிங்கிழங்குக்கு[72].

12.ELAM (fig 2.12)

Synonyms **:** Aanji, Korangam

Botanical name : Elettaria cardamomum

Suvai **:** Kaarppu

Thanmai : Veppam

Pirivu : Kaarppu

Action : Carminative

Stimulant

Stomachic

General characters:

தொண்டை வாய்கவுள் தாலுகு தங்களில்

தோன்றும் நோயதி சாரம்பன் மேகத்தால்

உண்டை போல்எழுங் கட்டி கிரிச்சரம்

உழலை வாந்தி சிலந்தி விஷஞ்சுரம்

பண்டை வெக்கை விதாகநோய் காசமும்

பாழுஞ் சோமப் பிணிவிந்து நட்டமும்

அண்டை யீளைவன் பித்தம் இவைக்கெல்லாம்

ஆல மாங்கமழ் ஏல மருந்ததே…(73)

Fig 2.1 VARITHUMATIKAI

Fig 2.2 VENGAYAM

Fig 2.3 ELUMITCHAI

Fig 2.4 CHITRAMANAKKU ENNAI

Fig 2.5 INJI

Fig 2.6 SEERAGAM

Fig 2.7 DHANIYA

Fig 2.8 SATHAKUPPAI

Fig 2.9 LAVANGAM

Fig 2.10 LAVANGAPATTAI

Fig 2.11 MANJAL

Fig 2.12 ELAM

Fig 2.13 KALINGATHI ENNAI

MATERIALS AND METHODS

MATERIALS AND METHODS

EXPERIMENTAL STUDY DESIGN

This prospective, observational open clinical trial was performed on PCOS patients at one centres affiliated with The Tamil Nadu Dr. M.G.R. Medical University, Chennai between 2016-2018.

The study was conducted in the department of medicine, Arignar Anna Hospital of Indian Medicine, Chennai and with the assistance of laboratory setup of the department of biochemistry, AAHIM, Chennai. All subjects were being considered for the treatment with trial drug.

The study was approved by Institutional Ethics Committee (IEC) and the approved number is GSMC-CH-ME-5/002/2016. The study was registered in Clinical Trials Registry India (CTRI) and the reference number is REF/2018/02/017330.

SELECTION OF SAMPLE SIZE

40 female patients in the age group 15-45 years.

SELECTED CRITERIA

INCLUSION CRITERIA:

Patients with the following criteria are included in the study

- Polycystic ovaries on ultrasound examination
- Irregular menstruation
- Dysmenorrhea
- Ovulation related infertility
- Oligomenorrhoea
- Hirsutism
- Acanthosis nigricans

EXCLUSION CRITERIA

Patients with the following criteria are excluded from the study

- Hemorrhagic cyst
- Chocolate cyst
- Endometriosis
- Pituitary / Adrenal disorders
- Tuberculosis of the ovary and uterus
- Congenital uterine defects
- Hyperthyroidism / Hypothyroidism

WITHDRAWAL CRITERIA

Patients who have not completed the trial period are withdrawn from the study.

EVALUATION OF CLINICAL PARAMETERS

Patients are clinically evaluated by the following parameters

HISTORY TAKING

Age, occupation, socio-economic status, complaints and its duration, menstrual history, marital history, family history, previous illness, personal habits, body mass index were recorded in the case sheet for every patient at the time of first visit to the op.

INVESTIGATIONS

All patients were subjected to the laboratory investigations before and after the treatment.

BLOOD CHEMISTRY

TC, DC, ESR, HB,

Blood Sugar (R)

Serum Cholesterol

URINE ANALYSIS

Albumin, Sugar, Deposits

RADIOGRAPHICAL FINDINGS OF ULTRASONOGRAM

- ✓ Whole abdomen and pelvis
- ✓ Follicular study

CLINICAL DIAGNOSIS BASED ON SIDDHA SYSTEM OF MEDICINE

The parameters used to diagnosis Soothaga vaayu based on Siddha system

- Poriyaalarithal
- Pulanaalarithal
- Vinathal
- Envagaithervugal
- Uyirthathukkal
- Udalthathukkal

RESULTS AND OBSERVATION

RESULTS AND OBSERVATION

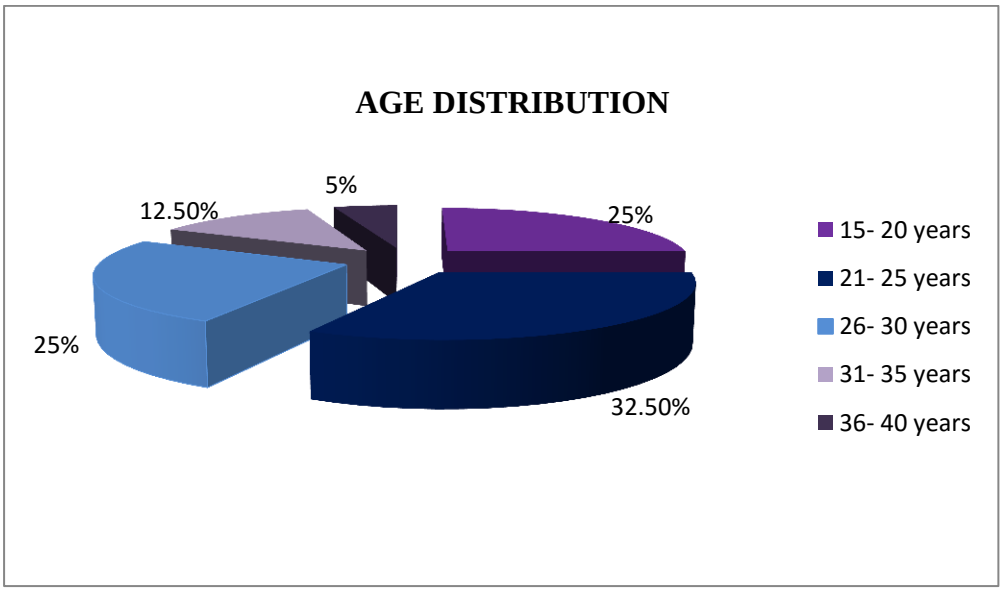
The study on Soothaga vaayu was carried out with 40 patients in the Out Patient Department, PG Maruthuvam, Govt Siddha Medical College attached to AAGHIM, Chennai-106, during the year 2016-2018 were analysed.

The observations were made and tabulated regarding the following criteria:

1. Age distribution
2. Distribution of Kaalam
3. Occupation (Nature of work)
4. Socio-economic status
5. Food habits
6. Marital status
7. Body mass index
8. Paruvakaalam
9. Thinai
10. Distribution of vatham
11. Distribution of pitham
12. Distribution of kabham
13. Defects in udal thathukkal
14. Envagai thervugal
15. Naadi
16. Neikuri
17. Signs and symptoms before and after treatment
18. Result

1. AGE DISTRIBUTION

AGE (YEARS)	NO OF CASES	PERCENTAGE (%)
15-20 years	10	25%
21-25 years	13	32.5%
26-30 years	10	25%
31-35 years	5	12.5%
36-40 years	2	5%

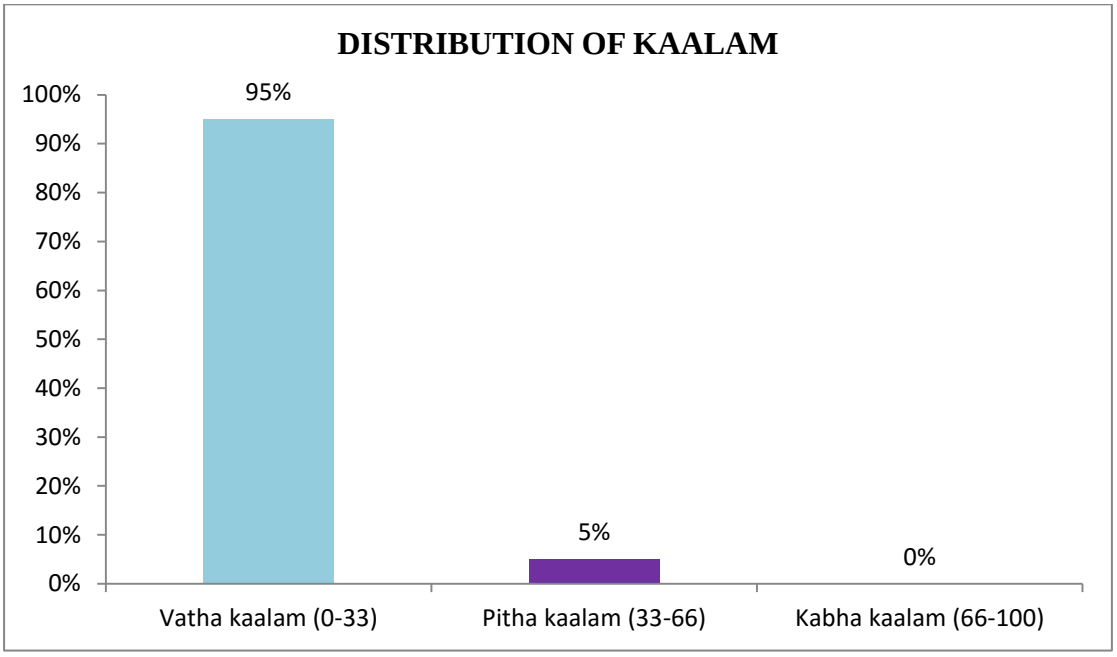


INFERENCE:

25% of patients were in the age group 15-20, 32.5% of patients were in the age group 21-25, 25% of patients were in the age group 26-30, 12.5% of patients were in the age group 31-35 and 5% of patients were in the age group 36-40.

2. DISTRIBUTION OF KAALAM

KAALAM	NO. OF CASES	PERCENTAGE
Vatha kaalam (0-33)	38	95%
Pitha kaalam (34-66)	2	5%
Kaabha kaalam (66-100)	0	0

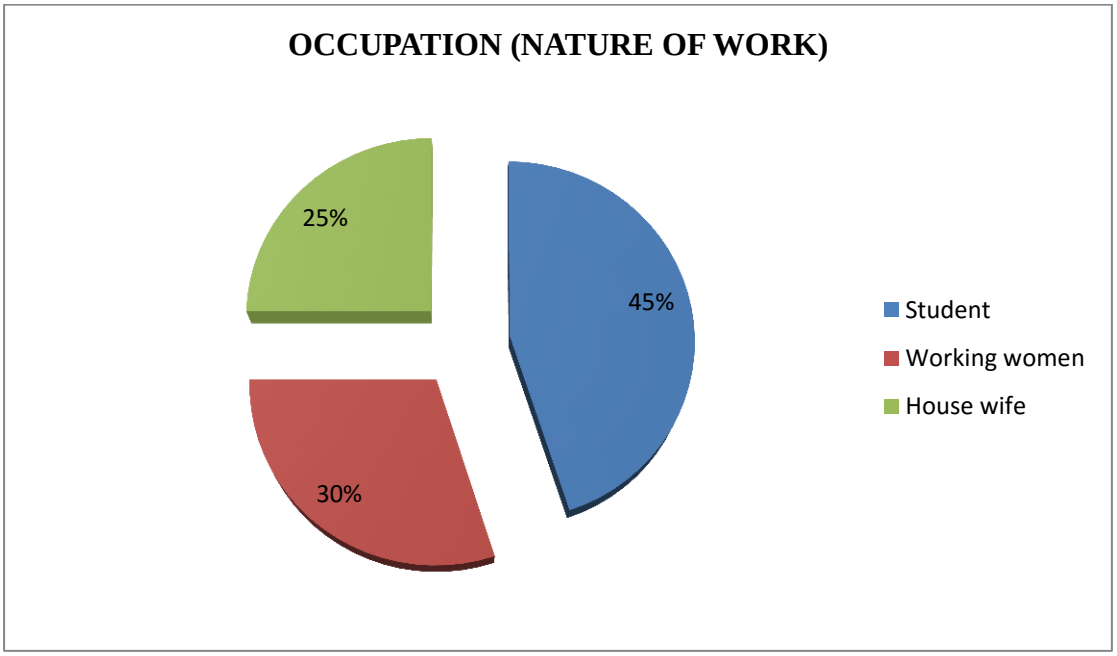


INFERENCE:

95% of patients were in vatha kaalam and 5% of patients were in pitha kaalam.

3. OCCUPATION (NATURE OF WORK)

WORK	NO.OFCASES	PERCENTAGE (%)
Student	18	45%
Working women	12	30%
House wife	10	25%

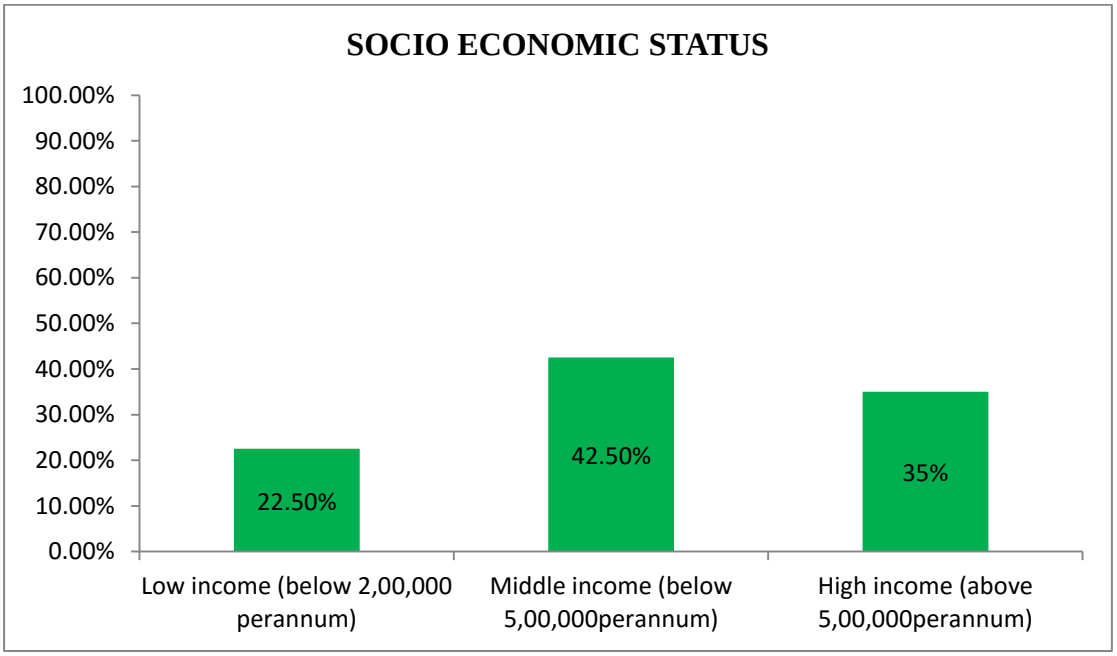


INFERENCE:

45% of patients were students, 30% of patients were working women and 25% of patients were house wife.

4. SOCIO ECONOMIC STATUS

SOCIOECONOMIC STATUS	NO.OF CASES	PERCENTAGE (%)
Low income (Below 2,00,000 perannum)	9	22.5%
Middle income (below 5,00,000 perannum)	17	42.5%
High income (above 5,00,000perannum)	14	35%

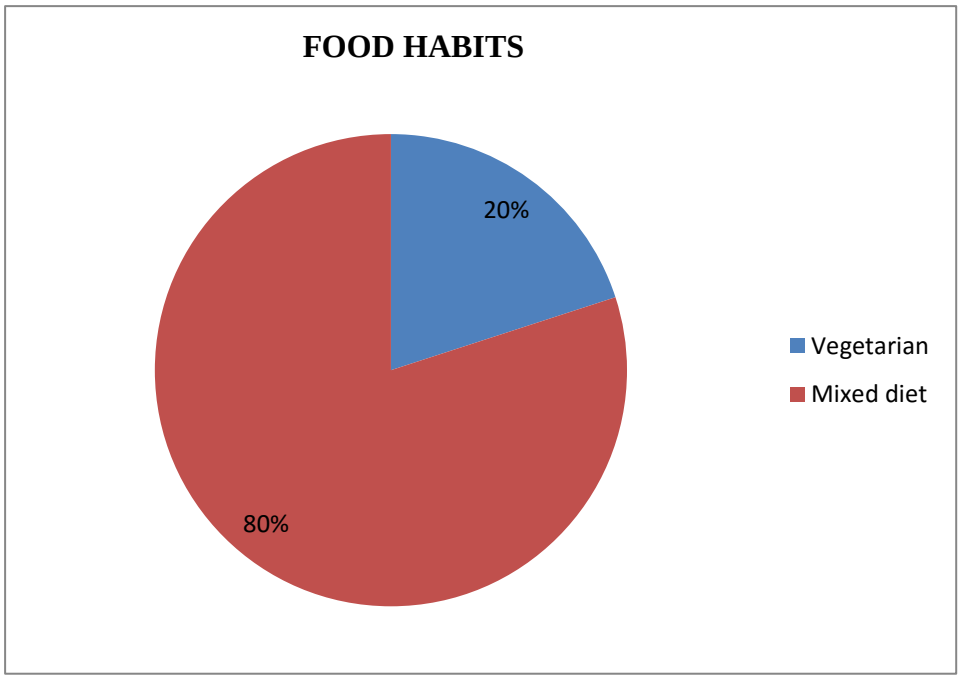


INFERENCE:

22.5% of patients were from low income group, 42.5% of patients were from middle income group, 35% of patients were from high income group.

5. FOOD HABITS

DIET	NO.OF CASES	PERCENTAGE (%)
Vegetarian	8	20%
Mixed diet	32	80%

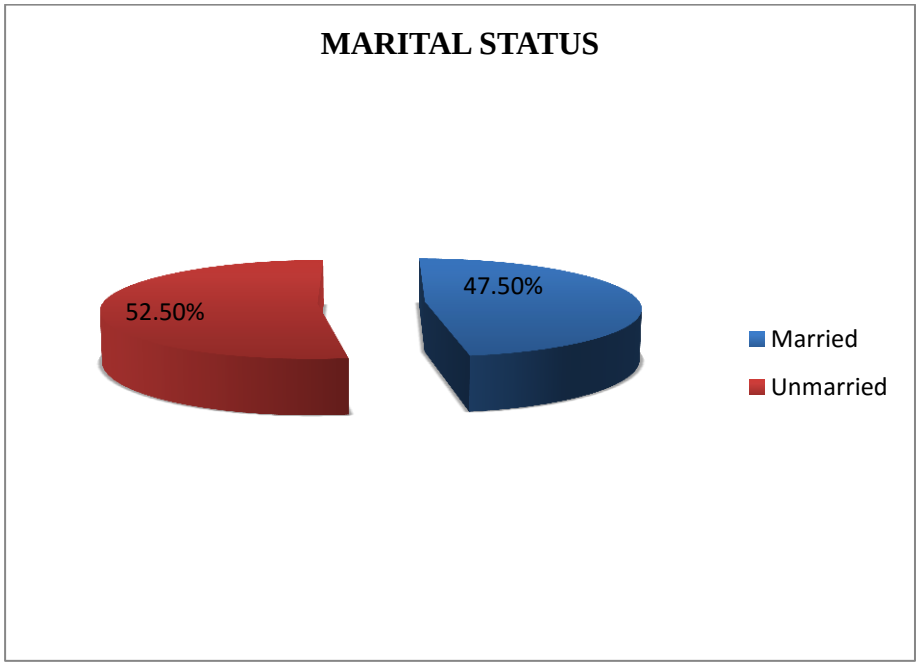


INFERENCE:

80% of patients belong to mixed diet and 15% of patients belong to vegetarian diet habit.

6. MARITAL STATUS

MARITAL STATUS	NO.OF CASES	PERCENTAGE (%)
Married	19	47.5%
Unmarried	21	52.5%

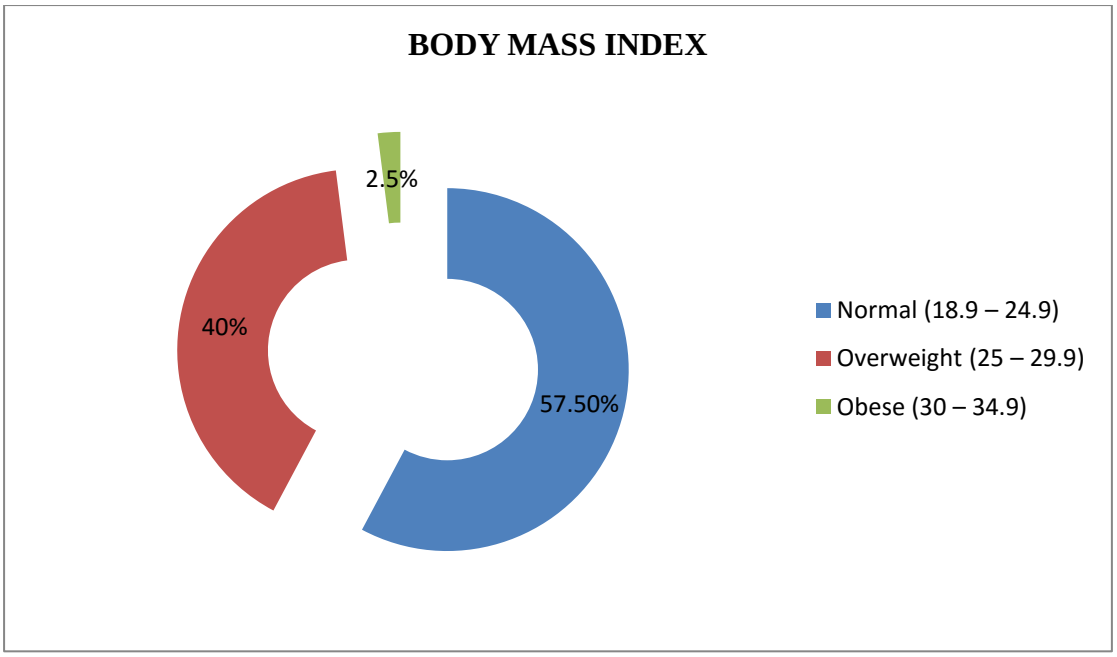


INFERENCE:

47.5% of patients were married and 52.5% of patients were unmarried.

7. BODY MASS INDEX

BMI (kg/m^2)	NO. OF CASES	PERCENTAGE (%)
Normal (18.9 – 24.9)	23	57.5%
Overweight (25 – 29.9)	16	40%
Obese (30 – 34.9)	01	2.5%

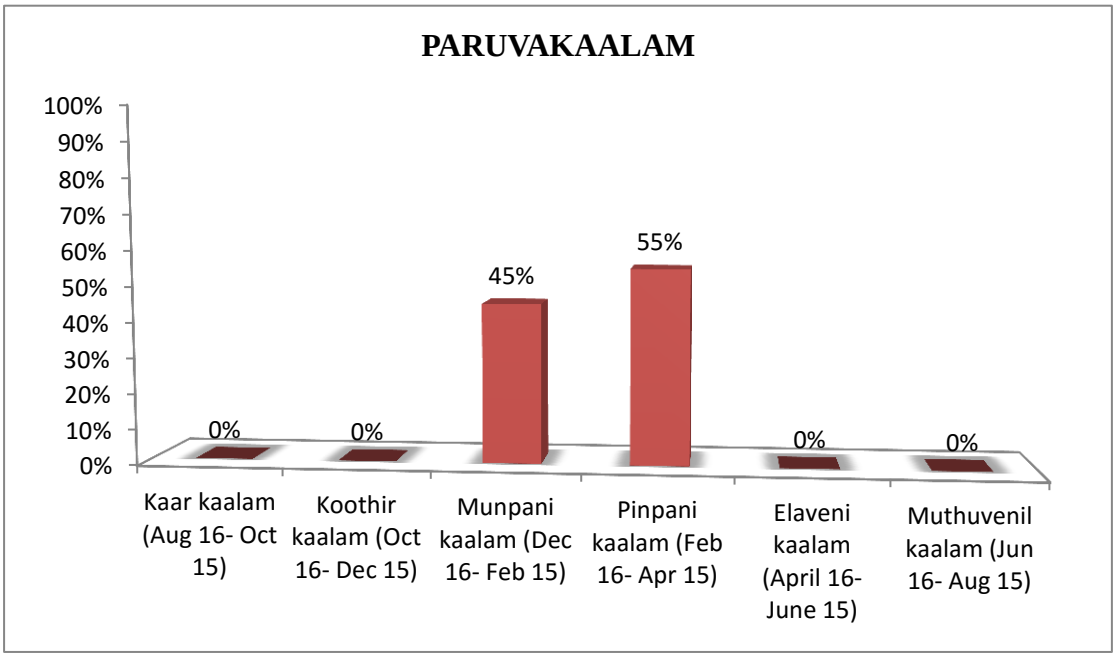


INFERENCE

57.50% of patients was normal (18.9-24.9 kg/m^2), 40% of patients was overweight (25-29.9 kg/m^2), and 2.5% of patient was obese (30-34.9 kg/m^2).

8. PARUVAKAALAM

KAALAM	NO.OF CASES	PERCENTAGE(%)
Kaar kaalam (Aug 16- Oct 15)	0	0
Koothir kaalam (Oct 16- Dec 15)	0	0
Munpani kaalam (Dec 16- Feb 15)	18	45%
Pinpani kaalam (Feb 16- Apr 15)	22	55%
Elaveni kaalam (April 16- June 15)	0	0
Muthuvenil kaalam (Jun 16- Aug 15)	0	0

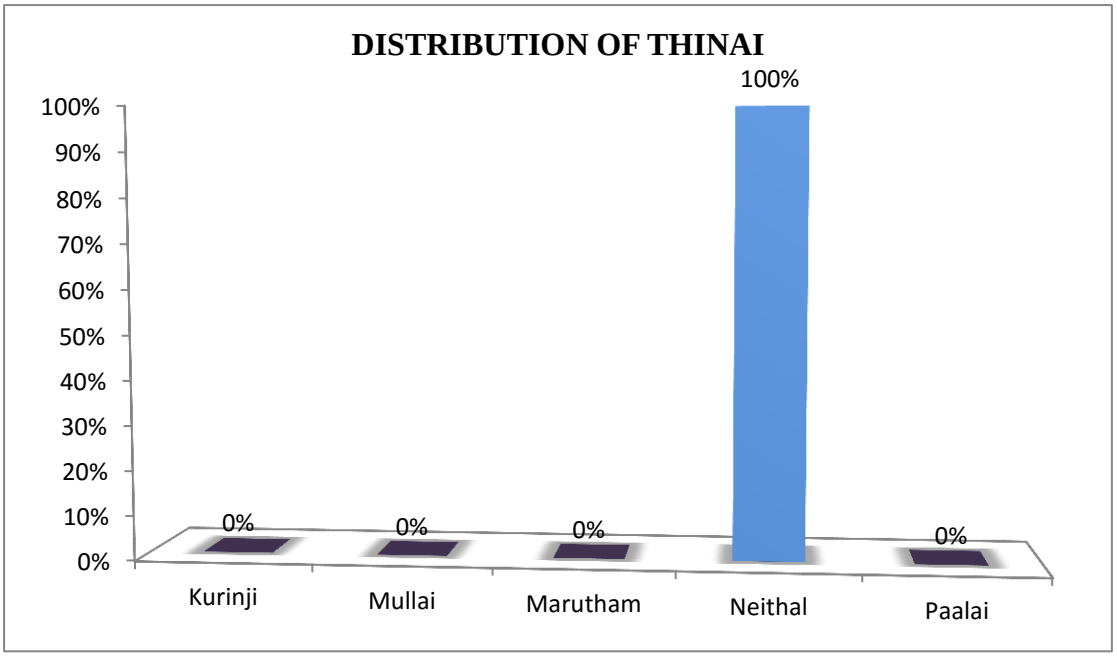


INFERENCE:

45% patients were reported in munpanikaalam and 55% patients were reported in pinpanikalam.

9. DISTRIBUTION OF THINAI

THINAI	NO.OF CASES	PERCENTAGE (%)
Kurinji	0	0%
Mullai	0	0%
Marudham	0	0%
Neithal	40	100%
Paalai	0	0%

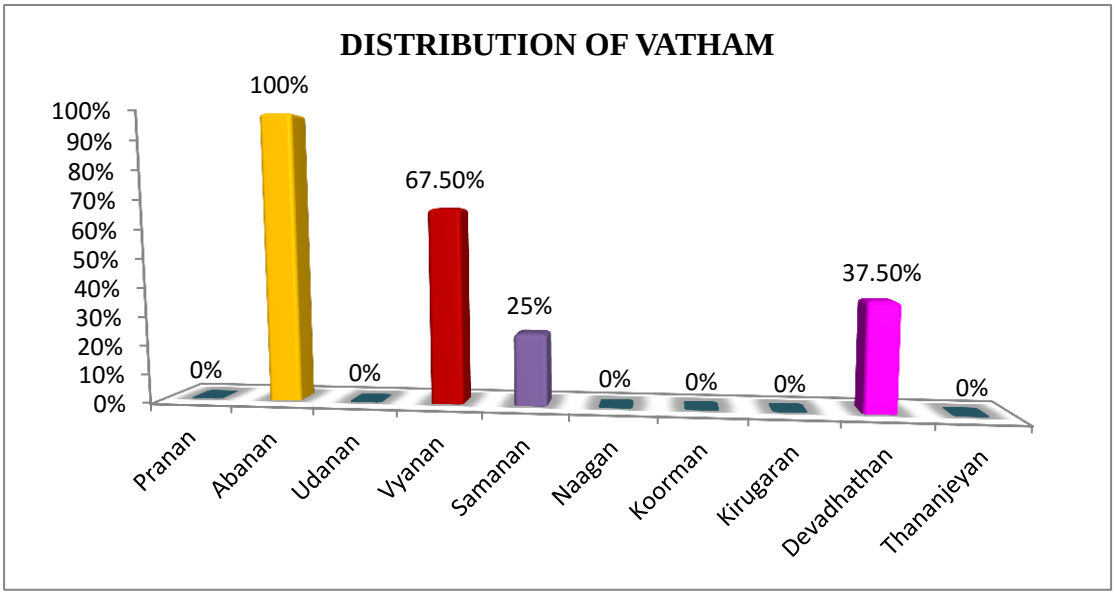


INFERENCE:

100% of patients were from Neithal thinai.

10. DISTRIBUTION OF VATHAM

VATHAM	NO.OF CASES	PERCENTAGE (%)
Pranan	0	0%
Abanan	40	100%
Udanan	0	0
Vyanan	27	67.5%
Samanan	10	25%
Naagan	0	0%
Koorman	0	0%
Kirugaran	0	0%
Devadhathan	15	37.5%
Thananjeyan	0	0

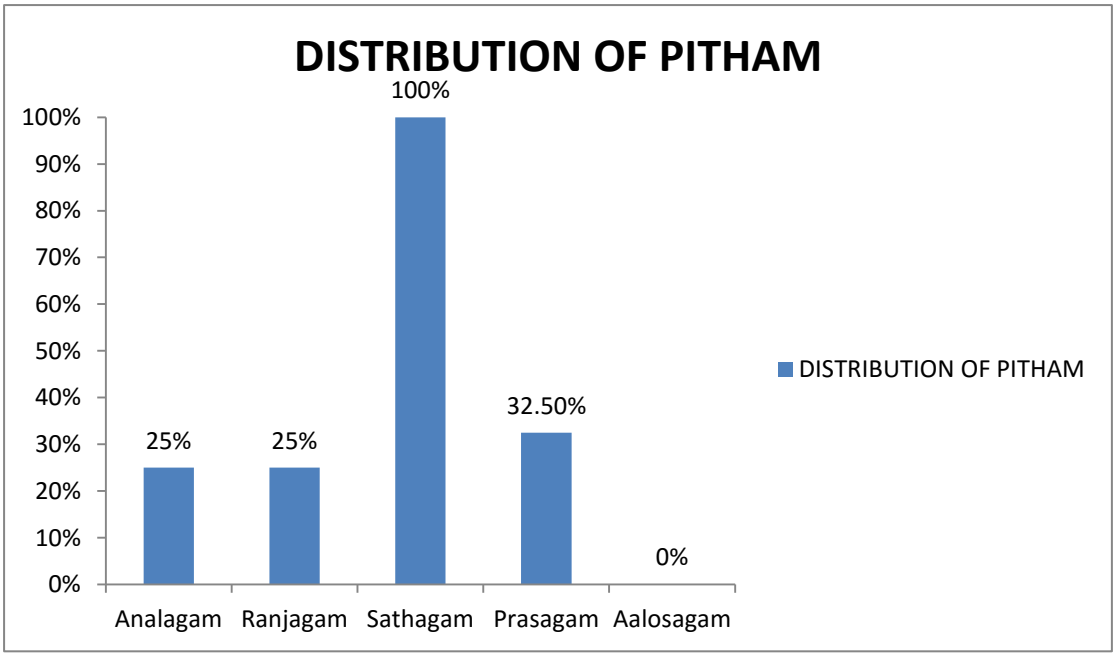


INFERENCE:

Abanan affected in 100% patients, Vyanan affected in 67.5% patients, Samanan affected in 25% patients, Devedhathan affected in 37.5% patients.

11. DISTRIBUTION OF PITHAM

PITHAM	NO.OF CASES	PERCENTAGE (%)
Analagam	10	25%
Ranjagam	10	25%
Sathagam	40	100%
Prasagam	13	32.5%
Aalosagam	0	0%

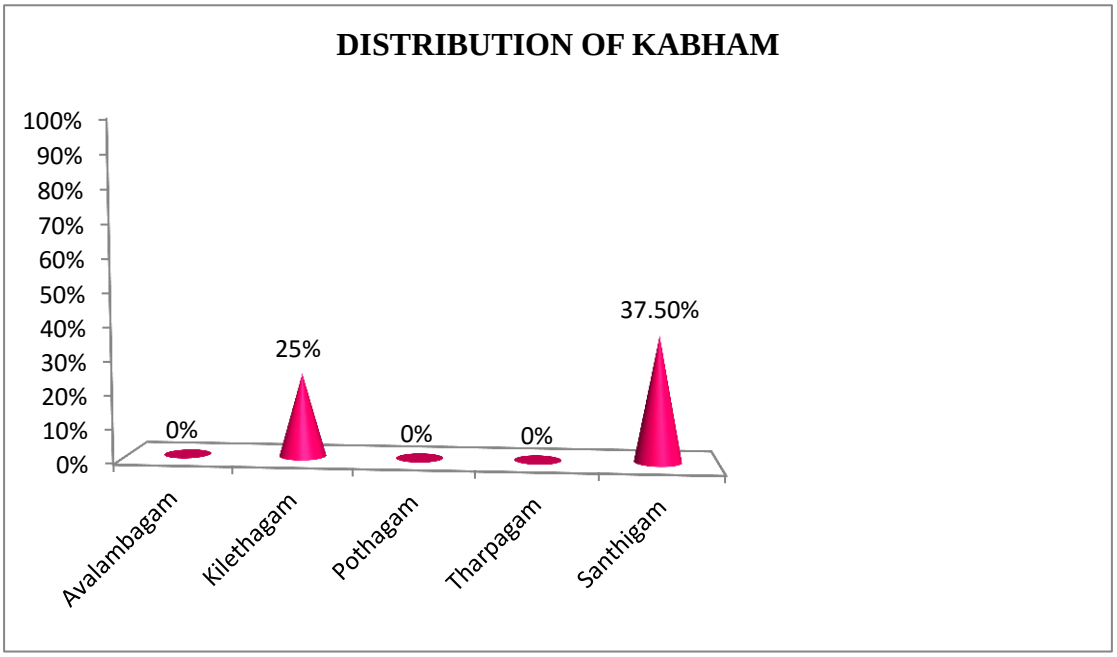


INFERENCE:

Analagam affected in 25% of patients, Ranjagam affected in 25% of patients, Sathagam affected in 100% patients and Prasagam affected in 32.5% of patients.

12. DISTRIBUTION OF KABHAM

KABHAM	NO.OF CASES	PERCENTAGE (%)
Avalambagam	0	0%
Kilethagam	10	25%
Pothagam	0	0%
Tharpagam	0	0%
Santhigam	15	37.5%

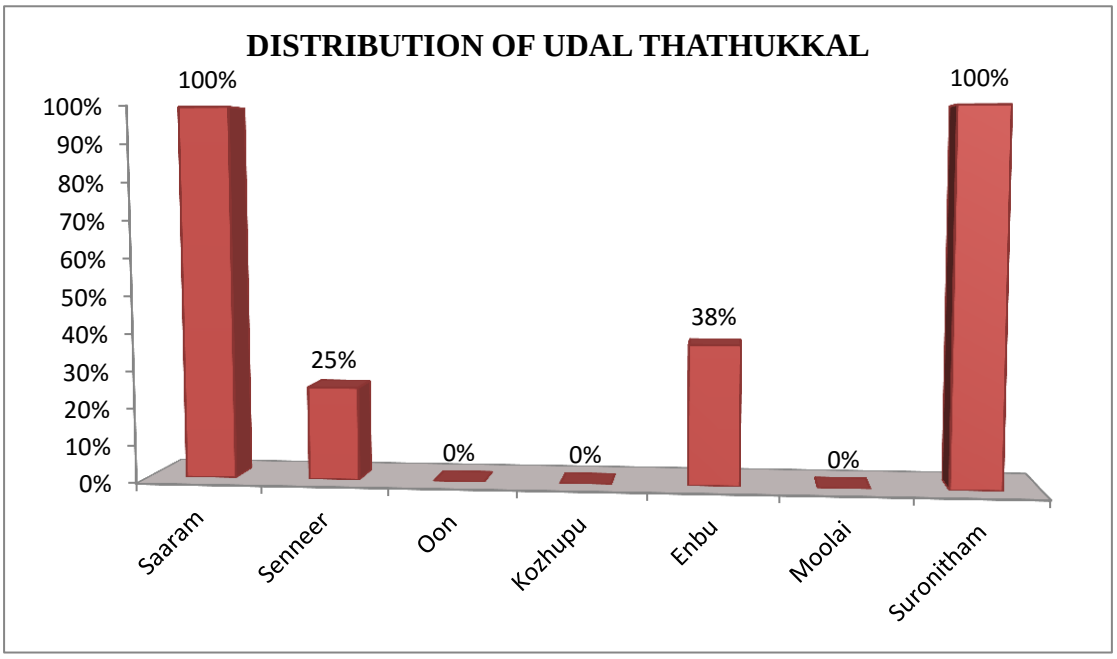


INFERENCE:

Santhigam was affected in 37.5% of patients and Kilethagam was affected in 25% of patients.

13. DISTRIBUTION OF UDAL THATHUKKAL

THATHUKKAL	NO.OF CASES	PERCENTAGE (%)
Saaram	40	100%
Senneer	10	25%
Oon	0	0%
Kozhupu	0	0%
Enbu	15	37.5%
Moolai	0	0%
Suronitham	40	100%

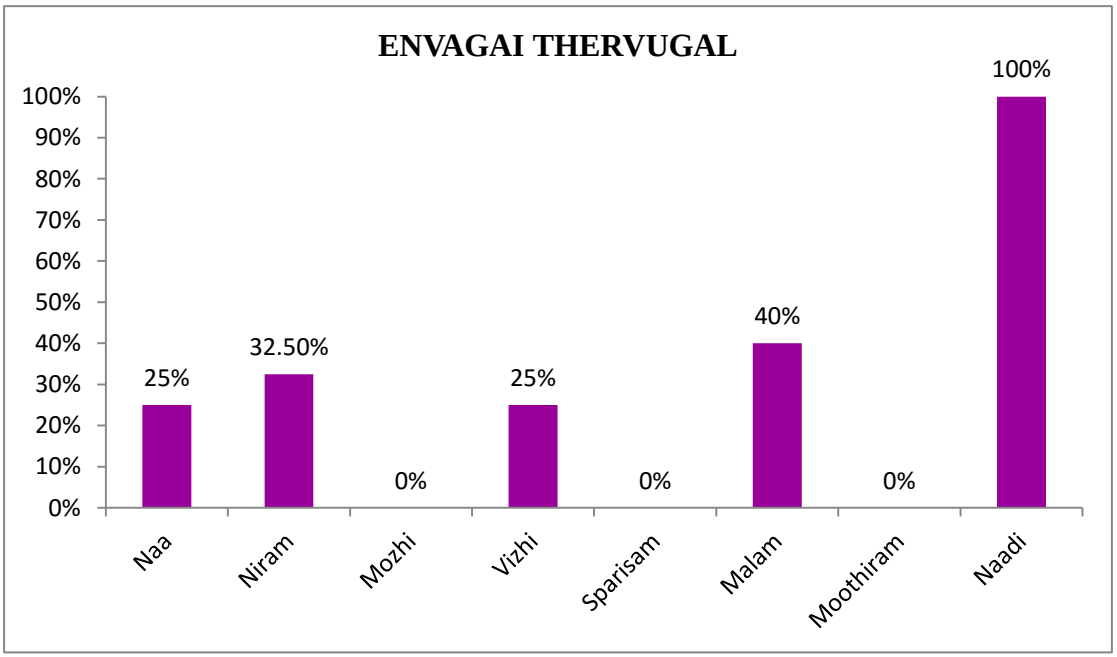


INFERENCE:

Suronitham and Saram were affected in all patients 100%, Enbu was affected in 38% of patients and Senneer was affected in 25% of patients.

14. ENVAGAI THERVUGAL

ENVAGAI THERVUGAL	NO.OF CASES	PERCENTAGE (%)
Naa	10	25%
Niram	13	32.5%
Mozhi	0	0%
Vizhi	10	25%
Sparisam	0	0%
Malam	16	40%
Moothiram	0	0%
Naadi	40	100%

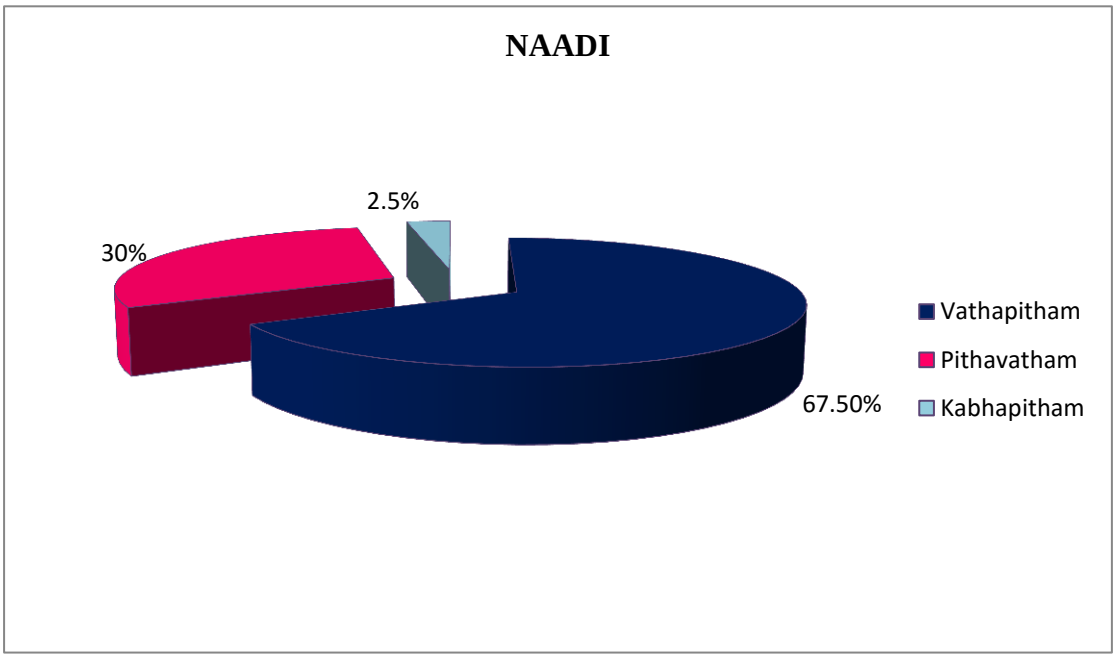


INFERENCE:

Naa affected in 25% of patients, Niram affected in 32.5% of patients, Vizhi affected in 25% of patients, Malam affected in 40% of patients, Naadi affected in 100% of patients.

15. DISTRIBUTION OF NAADI

NAADI	NO.OF CASES	PERCENTAGE (%)
Vatha pitham	27	67.5%
Pitha vatham	12	30%
Kabha pitham	1	2.5%

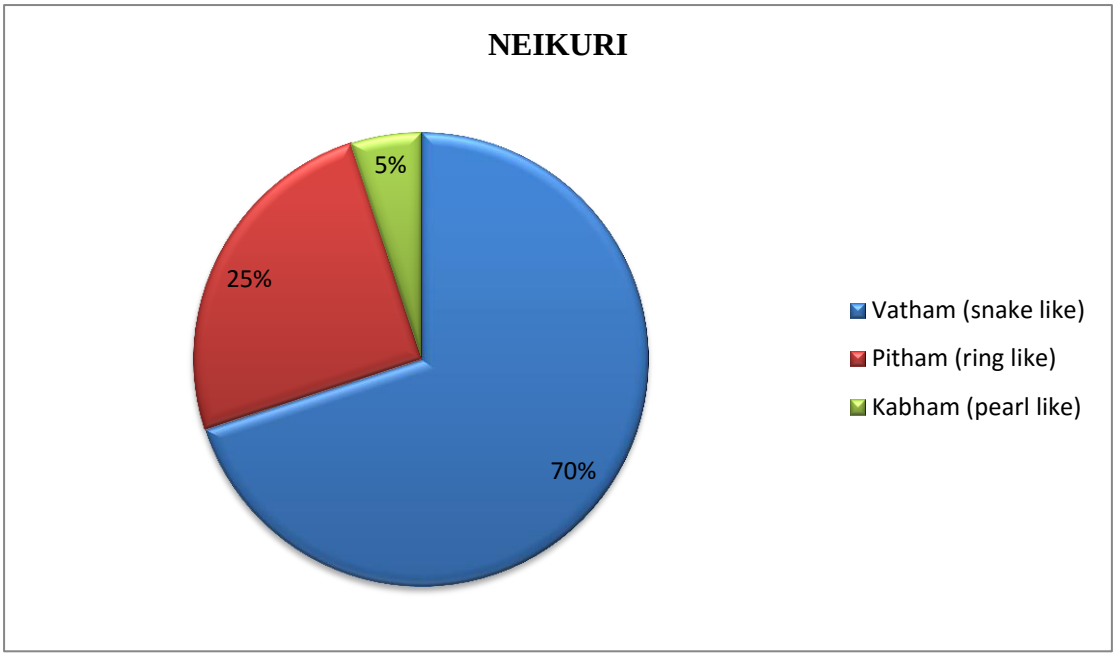


INFERENCE:

67.5% of patients had Vatha pitha Naadi, 30% of patients had Pitha vatha Naadi and 2.5% of patients had Kabha pitha Naadi.

16. NEIKURI

NEIKURI	NO.OF CASES	PERCENTAGE (%)
Vatham (snake like)	28	70%
Pitham (ring like)	10	25%
Kabham (pearl like)	02	5%

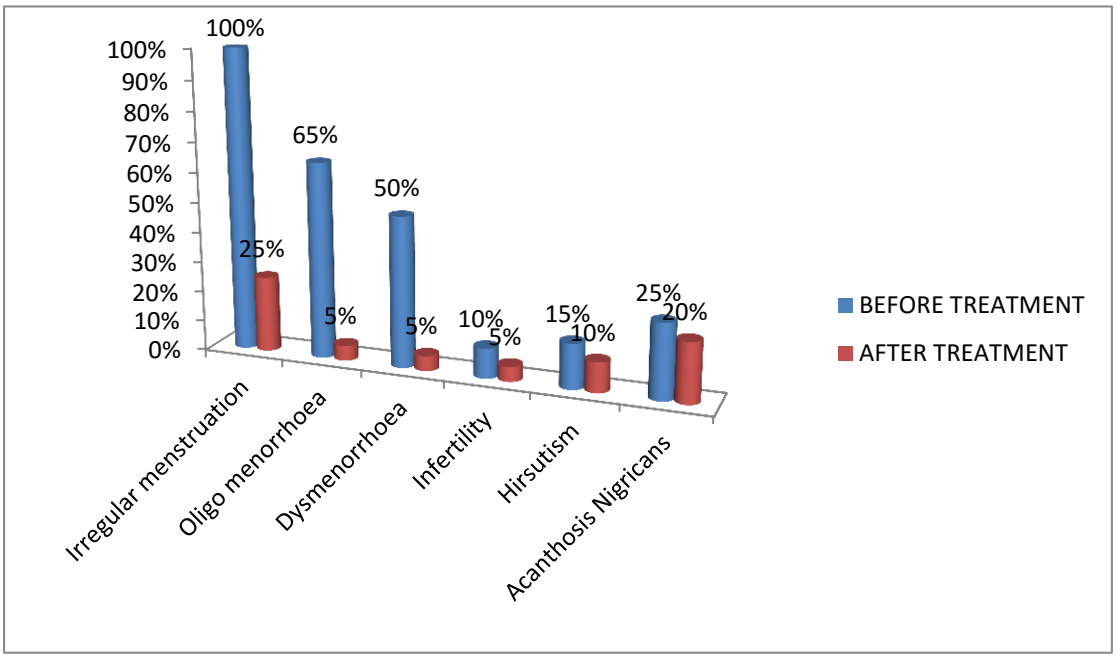


INFERENCE:

70% of patients had Vatha neer, 25% of patients had Pitha neer and 5% of patients had Kabha neer.

17. CLINICAL MANIFESTATIONS

SIGNS & SYMPTOMS	BEFORE TREATMENT		AFTER TREATMENT	
	NO.OF PATIENTS	PERCENTAGE (%)	NO.OF PATIENTS	PERCENTAGE (%)
Irregular menstruation	40	100%	10	25%
Oligo menorrhoea	26	65%	2	5%
Dysmenorrhoea	20	50%	2	5%
Infertility	4	10%	2	5%
Hirsutism	6	15%	4	10%
Acanthosis Nigricans	10	25%	8	20%

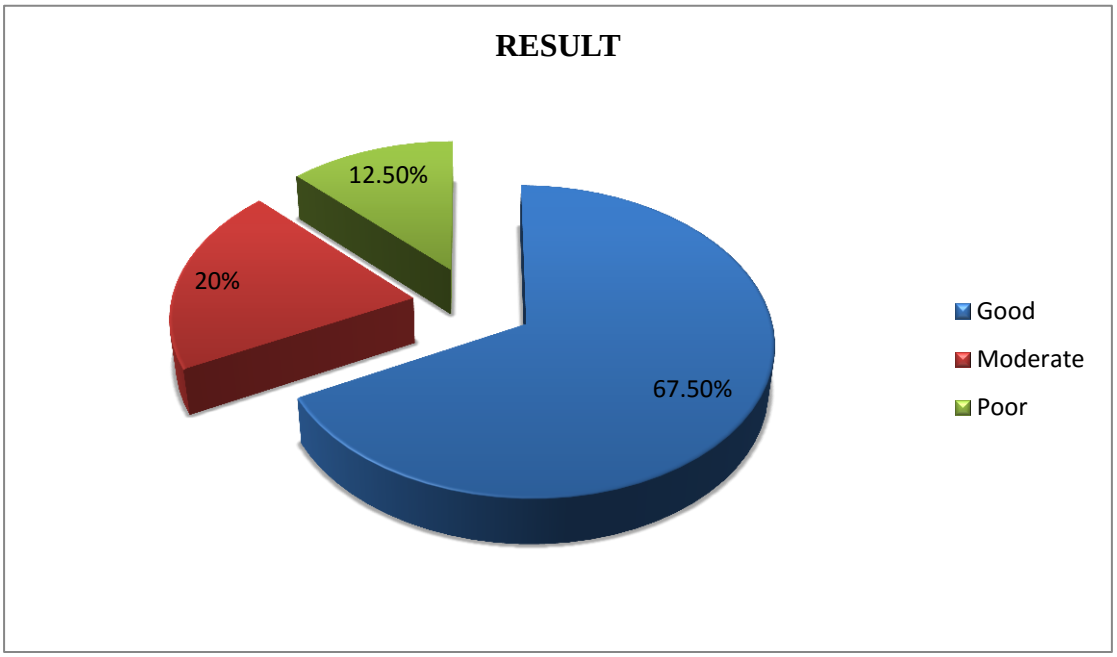


INFERENCE:

75% of patients were relived from irregular menstruation, 60% of patients were relieved from oligomenorrhoea, 45% of patients were relieved from dysmenorrhoea, 5% of patients were relived from hirsutism, 5% of patients were relieved from A.nigricans and 5% were conceived.

18.RESULT

RESULT	NO.OF CASES	PERCENTAGE (%)
Good	27	67.5%
Moderate	08	20%
Poor	05	12.5%



INFERENCE:

Out of 40 cases 27 (67.5%) had good result, 8 cases (20%) had moderate result and 5 cases (12.5%) had poor result.

RESULTS OF PATIENTS BEFORE AND AFTER TREATMENT

ULTRASONOGRAM REPORT

Sl.NO	OP NO	AGE/ SEX	DURATION OF CYCLES	OVARY VOLUME BT	OVARY VOLUME AT
1.	5052	21	3	RT - 12ml LT – 13ml	RT – 8ml LT – 6ml
2.	5090	24	3	RT – 16ml LT – 21ml	Both ovaries appear normal in size
3.	8765	32	3	RT – 9ml LT – 12ml	RT – 5ml LT – 6ml
4.	9138	22	3	RT – 30ml LT – 29ml	RT – 30ml LT – 28ml
5.	770	36	3	RT – 7ml LT – 9ml	RT – 6ml LT – 7ml
6.	787	17	3	RT – 14ml LT – 10ml	RT – 10ml LT – 6ml
7.	1022	18	3	RT – 14ml LT – 3ml	RT – 5ml LT – 6ml
8.	1522	21	3	RT – 20ml LT – 21ml	RT – 10ml LT – 12ml

9.	1840	33	3	RT – 12ml LT – 8ml	RT – 7ml LT – 5ml
10.	4670	20	3	RT – 30ml LT – 13ml	RT – 30ml LT – 13ml
11.	8555	29	3	RT – 37ml LT – 38ml	RT – 36ml LT – 37ml
12.	8763	32	3	RT – 23ml LT – 19ml	RT – 23ml LT – 18ml
13.	8818	20	3	RT – 13ml LT – 6ml	Both ovaries appear normal in size
14.	8900	19	3	RT – 10ml LT – 7ml	RT – 7ml LT – 5ml
15.	9012	25	3	RT – 10ml LT – 9ml	RT – 6ml LT – 7ml
16.	9765	27	3	RT – 9ml LT – 9ml	RT – 6ml LT – 5ml
17.	149	23	3	RT – 14ml LT – 13ml	RT – 15ml LT – 14ml
18.	325	24	3	RT – 12ml LT – 18ml	RT – 6ml LT – 7ml
19.	521	32	3	RT – 6ml LT – 11ml	RT – 5ml LT – 5ml

20.	1623	20	3	RT – 7ml LT – 6ml	RT – 6ml LT – 5ml
21.	1626	26	3	RT – 7ml LT – 5ml	RT – 6ml LT – 7ml
22.	1631	21	3	RT – 12ml LT - 15ml	RT – 12ml LT – 16ml
23.	1646	24	3	RT – 15ml LT – 21ml	RT – 12ml LT – 10ml
24.	2929	28	3	RT – 22ml LT – 16ml	RT – 22ml LT – 16ml
25.	3510	19	3	RT – 7ml LT – 9ml	RT – 6ml LT – 9ml
26.	3703	21	3	RT – 6ml LT – 4ml	RT – 5ml LT – 6ml
27.	4810	20	3	RT – 22ml LT – 18ml	RT – 10ml LT – 12ml
28.	5015	26	3	RT – 8ml LT – 7ml	RT – 6ml LT – 5ml
29.	5514	15	3	RT – 10ml LT – 9ml	RT – 9ml LT – 7ml
30.	5739	21	3	RT – 24ml LT – 19ml	RT – 24ml LT – 19ml

31.	5842	29	3	RT – 16ml LT – 7ml	RT – 16ml LT – 6ml
32.	8874	27	3	RT – 10ml LT – 8ml	RT – 5ml LT – 8ml
33.	8980	25	3	RT – 18ml LT – 14ml	RT – 18ml LT – 14ml
34.	9970	32	3	RT – 19ml LT – 23ml	RT – 13ml LT – 18ml
35.	341	26	3	RT – 20ml LT – 21ml	RT – 12ml LT – 16ml
36.	1298	34	3	RT – 10ml LT – 16ml	RT – 10ml LT – 16ml
37.	1462	38	3	RT – 8ml LT – 6ml	RT – 8ml LT – 4ml
38.	1488	30	3	RT – 11ml LT – 16ml	RT – 12ml LT – 15ml
39.	1537	22	3	RT – 10ml LT – 7ml	RT – 10ml LT – 7ml
40.	1592	15	3	RT – 10ml LT – 9ml	RT – 11ml LT – 8ml

FOLLICULAR STUDY REPORT

Sl.NO	OP NO	AGE / SEX	FOLLICULAR STUDY BT	FOLLICULAR STUDY AT	REMARKS
1.	5052	21	Anovulatory cycle	Dominant follicle seen	Completed
2.	5090	24	Anovulatory cycle	Dominant follicle seen	Completed
3.	8765	32	Anovulatory cycle	Dominant follicle seen	Completed
4.	9138	22	Anovulatory cycle	No dominant follicles	Symptoms reduced
5.	770	36	Anovulatory cycle	Dominant follicle seen	Completed
6.	787	17	Anovulatory cycle	Dominant follicle seen	Completed
7.	1022	18	Anovulatory cycle	Dominant follicle seen	Completed
8.	1522	21	Anovulatory cycle	Dominant follicle seen	Completed
9.	1840	33	Anovulatory cycle	Dominant follicle seen	Completed
10.	4670	20	Anovulatory cycle	No dominant follicles	No changes

11.	8555	29	Anovulatory cycle	No dominant follicles	Symptoms reduced
12.	8763	32	Anovulatory cycle	No dominant follicles	Symptoms reduced
13.	8818	20	Anovulatory cycle	Dominant follicle seen	Completed
14.	8900	19	Anovulatory cycle	Dominant follicle seen	Completed
15.	9012	25	Anovulatory cycle	Dominant follicle seen	Completed
16.	9765	27	Anovulatory cycle	Dominant follicle seen	Completed
17.	149	23	Anovulatory cycle	No dominant follicles	Symptoms reduced
18.	325	24	Anovulatory cycle	Dominant follicle seen	Completed
19.	521	32	Anovulatory cycle	Dominant follicle seen	Completed
20.	1623	20	Anovulatory cycle	Dominant follicle seen	Completed
21.	1626	26	Anovulatory cycle	Dominant follicle seen	Completed
22.	1631	21	Anovulatory cycle	No dominant follicles	Symptoms reduced
23.	1646	24	Anovulatory cycle	Dominant follicle	Completed

				seen	
24.	2929	28	Anovulatory cycle	No dominant follicles	No changes
25.	3510	19	Anovulatory cycle	Dominant follicle seen	Completed
26.	3703	21	Anovulatory cycle	Dominant follicle seen	Completed
27.	4810	20	Anovulatory cycle	Dominant follicle seen	Completed
28.	5015	26	Anovulatory cycle	Dominant follicle seen	Completed
29.	5514	15	Anovulatory cycle	Dominant follicle seen	Completed
30.	5739	21	Anovulatory cycle	No dominant follicles	No changes
31.	5842	29	Anovulatory cycle	No dominant follicles	Symptoms reduced
32.	8874	27	Anovulatory cycle	Dominant follicle seen	Completed
33.	8980	25	Anovulatory cycle	No dominant follicles	No changes
34.	9970	32	Anovulatory cycle	Dominant follicle seen	Completed
35.	341	26	Anovulatory cycle	Dominant follicle seen	Completed

36.	1298	34	Anovulatory cycle	No dominant follicles	No changes
37.	1462	38	Anovulatory cycle	Dominant follicle seen	Completed
38.	1488	30	Anovulatory cycle	No dominant follicles	Symptoms reduced
39.	1537	22	Anovulatory cycle	Dominant follicle seen	Completed
40.	1592	15	Anovulatory cycle	No dominant follicles	Symptoms reduced

BLOOD INVESTIGATION AND RESULTS

SL NO	OP NO	BEFORE TREATMENT						AFTER TREATMENT					
		TC	DC			ESR(mm)		TC	DC			ESR(mm)	
		(cu/mm)	P%	L%	E%	1/2	1	(cu/mm)	P%	L%	E%	1/2	1
1.	5052	9100	71	25	4	5	10	8900	62	32	6	10	16
2.	5090	6400	67	32	1	7	15	7600	54	42	4	20	60
3.	8765	10900	54	39	7	10	8	9800	64	35	1	4	8
4.	9138	8900	59	38	3	12	25	9200	58	40	2	13	26
5.	770	8100	60	33	7	30	65	8000	62	36	2	4	9
6.	787	14500	81	16	3	30	70	14500	70	25	5	8	12
7.	1022	10900	61	34	5	12	25	9800	60	34	6	4	9
8.	1522	9300	65	30	5	14	29	8700	61	35	4	7	14
9.	1840	8200	55	41	4	2	8	8300	68	32	0	4	9
10.	4670	8200	60	36	4	5	12	9000	65	32	3	6	12
11.	8555	9700	54	42	4	5	12	9800	64	35	1	4	8
12.	8763	7600	59	39	2	7	14	8800	64	32	4	5	12
13.	8818	7900	64	31	5	10	22	8200	63	35	2	4	9
14.	8900	7800	59	37	4	8	12	8700	50	44	6	8	13
15.	9012	9100	62	41	2	8	14	9700	60	38	2	6	9
16.	9765	8000	56	39	5	15	28	8000	62	36	2	4	9
17.	149	6900	55	40	5	22	40	7200	65	35	0	12	20
18.	325	9000	51	45	4	5	13	9600	55	45	3	4	12
19.	521	7400	56	41	3	6	12	8600	57	40	3	5	12
20.	1623	9300	64	29	7	5	13	9600	55	42	3	4	12
21.	1626	7800	59	38	3	5	12	8300	61	35	4	7	14

22.	1631	8700	65	31	4	20	48	7600	60	36	4	3	10
23.	1646	6900	71	26	3	9	29	7000	64	35	1	9	18
24.	2929	7800	56	40	4	10	22	6900	52	43	5	7	12
25.	3510	10500	69	29	2	8	15	10600	57	40	3	8	20
26.	3703	8100	58	37	5	25	56	8000	53	42	5	12	24
27.	4810	8500	56	39	5	12	20	8700	65	30	5	5	9
28	5015	9400	71	25	4	14	21	8500	68	27	5	16	26
29.	5514	9000	72	24	4	6	12	9200	68	29	3	8	16
30.	5739	6300	61	34	5	13	25	8300	52	42	6	10	20
31.	5842	7600	50	44	6	2	7	8700	52	42	6	2	7
32.	8874	8900	61	34	5	7	15	8800	62	36	2	4	9
33.	8980	7500	67	31	2	18	40	7900	68	30	2	18	34
34.	9970	10500	64	32	4	13	26	10200	52	40	8	18	28
35.	341	6600	67	28	5	10	22	7500	72	26	2	6	11
36.	1298	10500	61	33	6	36	25	10500	67	30	3	12	18
37.	1462	8500	57	40	3	5	15	7800	56	41	3	5	12
38.	1488	8700	62	36	2	5	12	8600	58	38	4	6	14
39.	1537	7000	52	43	5	3	6	7700	58	38	4	4	10
40.	1592	7300	54	36	10	14	26	7200	56	36	8	15	23

TC : TOTAL COUNT

DC: DIFFERENTIAL COUNT

ESR: ERYTHROCYTE SEDIMENTATION RATE

SL NO	OP NO	BEFORE TREATMENT			AFTER TREATMENT			URINE		
		SU	HB	CHOL	SU	HB	CHOL	A	S	D
		(mg/dl)	(%)	(mg/dl)	(mg/dl)	(%)	(mg/dl)			
1.	5052	63	12.2	114	94	12.5	138	N	N	N
2.	5090	90	10.4	165	115	10.2	130	N	N	N
3.	8765	80	12.5	156	100	12.5	164	N	N	N
4.	9138	81	11.6	120	112	11.4	119	N	N	N
5.	770	98	9.7	152	110	10.2	150	N	N	N
6.	787	101	10.4	130	106	11.1	152	N	N	N
7.	1022	82	9.8	112	108	10.5	125	N	N	N
8.	1522	82	12.1	184	90	12.5	172	N	N	N
9.	1840	96	9.8	190	98	10	189	N	N	N
10.	4670	98	11.2	189	100	11.4	190	N	N	N
11.	8555	99	10.6	156	101	10.8	164	N	N	N
12.	8763	120	10.2	117	121	10.2	123	N	N	N
13.	8818	112	11.6	180	120	11.2	178	N	N	N
14.	8900	77	8.4	160	120	11	156	N	N	N
15.	9012	87	10.6	120	100	13.3	130	N	N	N
16.	9765	80	11	152	110	11	150	N	N	N
17.	149	120	11.1	156	110	10.8	145	N	N	N
18.	325	98	12.8	198	112	12.9	194	N	N	N
19.	521	89	12.1	160	92	12.1	140	N	N	N
20.	1623	98	13.8	198	112	12.9	194	N	N	N
21.	1626	82	10	184	90	11.1	190	N	N	N

22.	1631	110	12.1	152	91	12.1	155	N	N	N
23.	1646	120	13.5	153	124	12.1	140	N	N	N
24.	2929	83	10.1	185	110	12.9	194	N	N	N
25.	3510	72	12.2	135	110	11.1	190	N	N	N
26.	3703	88	13.4	170	90	12.1	155	N	N	N
27.	4810	113	12.4	163	110	13.4	156	N	N	N
28	5015	113	12	169	116	10.9	165	N	N	N
29.	5514	104	8.2	162	112	13.2	140	N	N	N
30.	5739	72	11.3	178	94	13.2	167	N	N	N
31.	5842	107	10.4	174	107	12.6	150	N	N	N
32.	8874	109	11.6	157	108	12.5	160	N	N	N
33.	8980	115	10	120	110	9.5	158	N	N	N
34.	9970	68	10.8	138	95	11.5	175	N	N	N
35.	341	90	12.4	135	116	10.4	153	N	N	N
36.	1298	79	11.0	147	112	11.4	158	N	N	N
37.	1462	90	10.3	153	87	10.4	125	N	N	N
38.	1488	90	12.8	136	104	11	135	N	N	N
39.	1537	110	9.8	158	104	12.4	140	N	N	N
40.	1592	102	10.5	156	106	11.6	153	N	N	N

SU: SUGAR

A: ALBUMIN

CHOL: CHOLESTEROL

S: SUGAR

HB: HEMOGLOBIN

D: DEPOSIT

DISCUSSION

DISCUSSION

SOOTHAGA VAAYU, one of the clinical entity described in Aathmaratchamirtham ennum vaidhiya sangiragam can be compared with Poly Cystic Ovarian Syndrome. The classical clinical features are Irregular menstruation, Dysmenorrhoea, Oligomenorrhoea, Hirsutism, Acanthosis nigricans, Infertility.

POLYCYSTIC OVARIAN SYNDROME is one of the most common female endocrine disorder. It's a complex, heterogenous disorder of uncertain aetiology. It affects 5-26% of women nowadays, like one in every three women especially in the reproductive age group affected by polycystic ovarian syndrome.

It is the most common cause for infertility. But there is no complete and satisfactory relief from their symptoms by other systems of medicine. Hence with the help of trial medicine the study was conducted in Arignar Anna Government Hospital of Indian Medicine attached to Government Siddha Medical College, Arumbakkam, Chennai, Tamilnadu, India. Hence 40 female patients with Soothaga vaayu were selected.

The Trial medicine KALINGATHI ENNAI was administered 15ml once a day with warm water before food for 5days for three consecutive menstrual cycles.

With the help of trail medicine from Siddha system, results and observations are noted for this study. The patients were examined based on Siddha and as well as Modern aspects.

All the necessary investigations were made during the study. The results obtained from their studies were discussed below for better conclusion.

DRUG AUTHENTICATION:

Authentication of given specimen is the basic starting point in developing a botanical product.

A sample of specimen is collected from raw drug store and its Organoleptic characters, Microscopic and Macroscopic examination was conducted and authenticated by Botanist, CCRS, Chennai.

PHYSIOCHEMICAL ANALYSIS:

Physiochemical parameters include

Loss on drying at 70^0C	-	8.20
Water soluble ash	-	8.75
Acid insoluble ash	-	0.85
Water soluble extractive value	-	7.20
pH analysis	-	6.540

These values of the given sample were compared with the standard values of Indian pharmacopeia.

PHARMACOLOGICAL EVALUATION:

The experimental protocol was approved by The Institutional Animal Ethics Committee of C.L. Baid Metha College of Pharmacy, Chennai, Tamil Nadu, India.

IAEC NO: LI/14/CLBMCP/2017.

Pharmacological studies of the trial medicine Kalingathi Ennai showed OVULATION INDUCING ACTIVITY on tested animals.

TOXICOLOGICAL STUDIES:

Acute and sub acute toxicity studies for Kalingathi ennai were conducted.

Acute toxicity study of Kalingathi ennai reveals no mortality, no abnormal signs and no behavioural changes in rat at the dose upto 200mg/kg body weight.

Sub acute oral toxicity study reveals no significant changes in the body weight, organ weight and biochemical parameters.

The toxicological study results show that the trial medicine has no toxic effects and they are safe.

BIOCHEMICAL ANALYSIS:

Biochemical assays are needed to evaluate disease models and to drive biomarker analysis in translation medicine and clinical research.

Based on the analysis Kalingathi Ennai contains Reducing sugar.

IEC:

IEC has approved my trial medicine with the allowed sample size of 40 patients with combined gender.

IEC NO: GSMC-CH-ME-5/002/2016

CTRI:

The global mandate is to register all clinical trials prospectively, i.e. before the enrolment of the first patient. I have successfully registered my trial medicine by submitting the details and scientific data's to Clinical Trial Registry.

CTRI NO: CTRI/2018/03/012768

CLINICAL STUDY:

Clinical studies were conducted followed by CTRI registration with the sample size of 40 patients.

In my study, 40 patients with Soothaga Vaayu were selected in the Department of Maruthuvam, Government Siddha Medical College, attached to Arignar Anna Government Hospital for Indian Medicine, Arumbakkam, Chennai – 106.

All necessary investigations were carried out to all patients and trial medicine was given. The results of before and after treatment of all the patients were analysed and discussed below.

AGE DISTRIBUTION:

Out of 40 cases 13 patients (32.5%) were between 21-25 years, 10 patients (25%) were between 15-20 years and 26-30 years, 5 patients (12.5%) were between 31-35 years, 2 patients (5%) were between 36-40 years.

DISRIBUTION OF KAALAM:

Among 40 patients, 38 patients (95%) were reported in vatha kaalam, 2 patients (5%) were reported in pitha kaalam, and none of the patients were reported in kabha kaalam.

Majority of the patients were reported in their vatha kaalam (95%).

Soothaga vaayu which is resulting from the deranged vatha kutram has high incidence in vatha kaalam.

OCCUPATION:

From selected 40 cases, 18 patients (45%) were student, 12 patients (30%) were working women, 10 patients (25%) were housewife.

SOCIO ECONOMIC STATUS:

Regarding Socio Economic Status 17 patients (42.5%) were from middle income, 14 patients (35%) were from high income, 9 patients (22.5%) were from low income.

FOOD HABITS:

Out of 40 cases, most of the cases 32 (80%) were taken mixed diet, and 8 cases (20%) had vegetarian diet only.

MARITAL STATUS:

Regarding marital status 21 patients (52.5%) were unmarried and 19 patients (47.5%) were married.

PARUVAKAALAM:

According to Paruvakaalam highest incidence of 22 cases (55%) were noted in Pinpani kaalam and 18 cases (45%) were noted in Munpani kaalam.

DISTRIBUTION OF THINAI:

According to the study, all 40 cases (100%) were from Neithal thinai. Neithal nilam was more prone to vatha disease.

DISTRIBUTION OF VATHAM:

In all the 40 patients (100%) Abanan was affected resulting in irregular menstruation, constipation in some patients and inability to conceive

In 27 patients (67.5%) Vyanan was affected causing tiredness, low back pain and lower abdominal pain.

Devadhathan was affected in 15 patients (37.5%) having disturbed sleep and psychological stress.

In 10 patients (25%) Samanan was affected resulting in loss of appetite.

DISTRIBUTION OF PITHAM:

Sathagapitham was affected in all cases producing irregular or absence of menstruation and inability to conceive.

In 13 patients (32.5%) Prasagam was affected causing hyper pigmentation of skin.

Analagam was affected in 10 patients (25%) causing loss of appetite.

Ranjagam was affected in 10 patients (25%) causing anaemia.

DISTRIBUTION OF KABHAM:

Santhigam was affected in 15 patients (37.5%) causing low back pain.

In 10 patients (25%) Kilethagam was affected causing loss of appetite.

DISTRIBUTION OF UDAL THATHUKKAL;

Suronitham was affected in all 40 patients (100%) resulting in irregular menstruation, lack of ovulation and inability to conceive.

Saaram was also affected in all 40 patients (100%) resulting in tiredness and loss of appetite.

Enbu was affected in 15 patients (37.5%) resulting in low back pain.

Senneer was affected in 10 patients (25%) resulting in pallor of skin, eye and reduced haemoglobin.

ENVAGAI THERVUGAL:

Naa was affected in 10 patients (25%) due to anaemic conditions (pale colour).

Niram was affected in 13 patients (32.5%) due to anaemia and hyperpigmentation in the neck and axillary region (Acanthosis Nigricans).

Vizhi was affected in 10 patients (25%) due to anaemic conditions (pale).

Malam was affected in 16 patients (40%) due to constipation.

Naadi was affected in all 40 patients (100%).

Naadi:

Out of 40 patients, 27 patients (67.5%) had Vatha Pitham, 12 patients (30%) had Pitha Vatham, 1 patient (2.5%) had Kabha Pitham.

NEIKURI:

Out of 40 patients 28 patients (70%) had Vatha Neer, 10 patients (25%) had Pitha Neer, 2 patients (5%) had Kabha Neer.

CLINICAL PROGNOSIS:

The clinical signs and symptoms were improved after treatment, showing only 10 cases (25%) had Irregular menstruation, 2 cases (5%) had Oligomenorrhoea, 2 cases (5%) had Dysmenorrhoea, 2 cases (5%) had Infertlity, 4 cases (10%) had Hirsutism, 8 cases (20%) had Acanthosis Nigricans.

INVESTIGATIONS:

Investigations like TC, DC, ESR, Hb, Serum cholesterol and Blood sugar were examined and urine analysis for albumin, sugar and deposits were also examined.

SPECIAL INVESTIGATION:

USG- abdomen and pelvis is advised for all the patients to confirm the diagnosis. USG pelvis was taken for all cases before treatment. They had bilateral polycystic ovaries.

Follicular study is advised for all patients.

After confirming the diagnosis, the patients were given the trial medicine and instructed to follow the diet and other restrictions based on Siddha system.

BIOSTATISTICAL STUDY:

Since the p value is *$p<0.005$;**$p<0.001$ significant in all clinical manifestations. So there is significant reducing of clinical manifestations among the patients for the treatment of it is concluded that the treatment was effective and significant.

RESULTS AFTER TREATMENT:

Clinical symptoms before and after treatment were noted to obtain prognosis of each clinical symptoms,

After treatment 75% of patients were relived from irregular menstruation, 60% of patients were relieved from oligomenorrhoea, 45% of patients were relieved from dysmenorrhoea, 5% of patients were relived from hirsutism, 5% of patients were relieved from A.nigricans.

This dessertation study aims to make regulate the menstrual cycle and has to induce dominant follicle.

OVERALL RESULT:

Out of 40 cases 27 (67.5%) had good result, 8 cases (20%) had moderate result and 5 cases (12.5%) had poor result.

SUMMARY

SUMMARY

The clinical study on Soothaga vaayu was carried out in Post graduate department of Pothu Maruthuvam, Government Siddha Medical College, Arignar Anna Hospital, Chennai – 106 during the period of 2015-2018.

A total of 40 patients were treated in the Outpatient department. The clinical and pathological assessment was carried out on the basis of Siddha and Modern aspects.

All the patients were treated with **Kalingathi Ennai** with warm water 15ml once a day, before food for 5 days, 3 consecutive menstrual cycles.

- Most of the patients were in the age group between 21-25 years (32.5%).
- Majority of the patients were reported in their vatha kaalam.
- 42.5% of the cases were in the Middle income group.
- 80% of the patients were Non-vegetarian.
- Most of the patients were affected in Pinpani kaalam (55%).
- Most of the patients were from Neithal thinai (100%).
- In vatham, Abanan (100%), Vyanan (67.5%), Devadhathan (37.5%), Samanan (25%) were affected.
- In Pitham, Sathagam (100%), Prasagam (32.5%), Analagam (25%), Ranjagam (25%) were affected.
- In Kabham, Santhigam (37.5%), Kilethagam (25%) were affected.
- In Ezhu udal kattugal, Saaram (100%), Senneer (25%), Enbu (37.5%), Suronitham (100%) were affected.

- In Envagai thervugal, Naa (25%), Niram (32.5%), Vizhi (25%), Malam (40%), Naadi (100%) were affected.

- Regarding Naadi, Vatha pitha naadi (67.5%) was the most common naadi observed.

- The toxicity study reveal that the trial medicine possesses no toxicity in animals. So it proved the safety of the trial medicine.

- The pharmacological study of the medicine shows that the medicine possesses ovulation inducing activity.

- Bio-statistical analysis of the clinical trial reveals significant p value < 0.005 and < 0.001and concluded that the treatment is effective and significant.

- The clinical trial shows that there is significant result in regulation of menstruation.

- Out of 40 cases 27 (67.5%) had good result, 8 cases (20%) had moderate result and 5 cases (12.5%) had poor result.

CONCLUSION

CONCLUSION

- **SOOTHAGA VAAYU** occurs due to derangement of vatham and pitham which affects menstruation.
- The trail medicine regularizes the menstrual cycle and induces ovulation. Thus it is beneficial in treating irregular menstruation and helps to regulate ovum maturation.
- The KALINGATHI ENNAI reveals no toxicity in the preclinical studies and hence proved to be safe for human administration.
- From the preclinical pharmacological study it is evident that, KALINGATHI ENNAI has significant ovulation inducing activity.
- No adverse effect was reported during the course of the treatment.
- From the clinical trial it is evident that the trial medicine regulates menstruation and induces dominant follicle.
- Hence I conclude that the Siddha trial medicine **KALINGATHI ENNAI** will be a better medicine that can be used in the treatment of **SOOTHAGA VAAYU**.

ANNEXURES

The Tamil Nadu Dr.M.G.R.Medical University

69, Anna Salai, Guindy, Chennai - 600 032.

This Certificate is awarded to Dr/Mr/Mrs.....S. BRUNDA.....

For participating as ~~Resource Person~~ / Delegate in the Twentieth Workshop on

"RESEARCH METHODOLOGY & BIOSTATISTICS"

For AYUSH Post Graduates & Researchers

Organized by the Department of Siddha

The Tamil Nadu Dr. M.G.R. Medical University From 07th to 11th March 2016.

Dr.N.KABILAN, M.D.(S)
PROF & HEAD
DEPT.OF SIDDHA

Prof.**Dr.P.ARUMUGAM,** M.D.,
REGISTRAR i/c

Prof. **Dr.S.GEETHALAKSHMI,** M.D., Ph.D.
VICE CHANCELLOR

सिद्ध केंद्रीय अनुसन्धान संस्थान
(सी.सी.आर.एस., चेन्नई, आयुष मंत्रालय, भारत सरकार)
अण्णा सरकारी अस्पताल परिसर, अरुम्बाक्कम, चेन्नई - 600106
SIDDHA CENTRAL RESEARCH INSTITUTE
(Central Council for Research in Siddha, Chennai,
Ministry of AYUSH, Government of India)
Anna Govt. Hospital Campus, Arumbakkam, Chennai - 600106
E-mail: crisiddha@gmail.com Phone: 044-26214925, 26214809

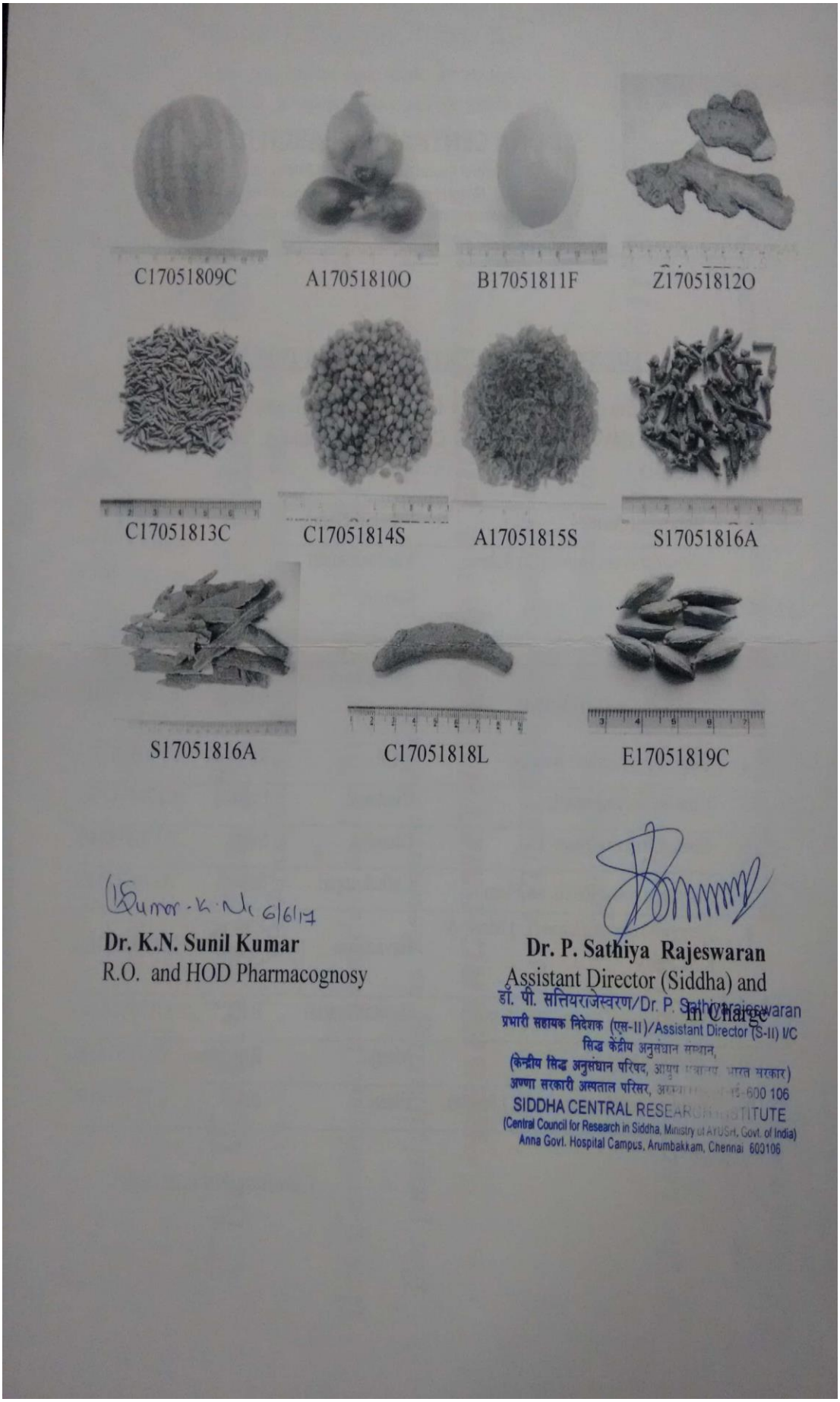
06.06.2017

AUTHENTICATION CERTIFICATE FOR 17051709-19

Certified that the drugs submitted by Dr. S. Brunda, MD (S) II Year, Dept of Maruthuvam, Govt. Siddha Medical College, Arumbakkam, Chennai-106 are identified as:

SN	Botanical Name	Tamil Name	Part	Code
1.	*Citrullus colocynthis* (L.) Schrad.	Varithummatti pazham	Fruit	C17051809C
2.	*Allium oschaninii* O.Fedtsch.	Venkayam	Bulb	A17051810O
3.	*Citrus limon* (L.) Osbeck.	Elumicham pazham	Fruit	C17051811L
4.	*Zingiber officinale* Roscoe	Inchi	Rhizome	Z17051812O
5.	*Cuminum cyminum* L.	Cirakam	Fruit	C17051813C
6.	*Coriandrum sativum* L.	Dhaniya	Seed	C17051814S
7.	*Anethum sowa* Roxb. ex Fleming	Cathakuppai	Seed	A17051815S
8.	*Syzygium aromaticum* (L.) Merr. & L.M.Perry	Ilavankam	Flower bud	S17051816A
9.	*Cinnamomum cassia* (L.) J. Presl	Ilavankapattai	Bark	C17051816V
10.	*Curcuma longa* L.	Manjal	Rhizome	C17051818L
11.	*Elettaria cardamomum* (L.) Maton.	Elam	Fruit	E17051819C

Continued in next page.....



6/6/17

Dr. K.N. Sunil Kumar
R.O. and HOD Pharmacognosy

Dr. P. Sathiya Rajeswaran
Assistant Director (Siddha) and
In Charge
डॉ. पी. सत्तियराजेस्वरण/Dr. P. Sathiyarajeswaran
प्रभारी सहायक निदेशक (एस-II)/Assistant Director (S-II) I/C
सिद्ध केंद्रीय अनुसंधान संस्थान,
(केन्द्रीय सिद्ध अनुसंधान परिषद, आयुष मंत्रालय, भारत सरकार)
अण्णा सरकारी अस्पताल परिसर, अरुम्बाक्कम, चेन्नै-600 106
SIDDHA CENTRAL RESEARCH INSTITUTE
(Central Council for Research in Siddha, Ministry of AYUSH, Govt. of India)
Anna Govt. Hospital Campus, Arumbakkam, Chennai 600106

C.L.BAID METHA COLLEGE OF PHARMACY

(An ISO 9001-2000 certified institute)

Jyothi Nagar, Old Mahabalipuram Road

Thoraipakkam, Chennai – 600 097

CERTIFICATE

This is to certify that the project entitled, Pharmacological and Toxicological screening of Kalingathi ennai submitted in partial fulfilment for the degree of M.D. (siddha) was carried out at C.L. Baid Metha college of Pharmacy, Chennai-97, in the Department of Pharmacology during the academic year of 2017-2018. It has been approved by the IAEC No: LI/14/CLBMCP/2017

C.L. Baid Metha College of Pharmacy CHENNAI-97 Thoraipakkam

Dr.P. MURALIDHARAN

IAEC MEMBER SECERATARY

ACUTE ORAL TOXICITY STUDY OF KALINGATHI ENNAI

(OECD GUIDELINE – 423)

Introduction:

- The acute toxic class method is a stepwise procedure with the use of 3 animals of a single sex per step.
- Depending on the mortality and/or the moribund status of the animals, on average 2-4 steps may be necessary to allow judgment on the acute toxicity of the test substance.
- This procedure is reproducible, uses very few animals and is able to rank substances in a similar manner to the other acute toxicity testing methods.
- The acute toxic class method is based on biometric evaluations with fixed doses, adequately separated to enable a substance to be ranked for classification purposes and hazard assessment.
- In principle, the method is not intended to allow the calculation of a precise LD50, but does allow for the determination of defined exposure ranges where lethality is expected since death of a proportion of the animals is still the major endpoint of this test.
- The method allows for the determination of an LD50 value only when at least two doses result in mortality higher than 0% and lower than 100%.
- The use of a selection of pre-defined doses, regardless of test substance, with classification explicitly tied to number of animals observed in different states improves the opportunity for laboratory to laboratory reporting consistency and repeatability.

Principle of the Test:

It is the principle of the test that based on a stepwise procedure with the use of a minimum number of animals per step, sufficient information is obtained on the acute toxicity of the test substance to enable its classification. The substance is administered orally to a group of experimental animals at one of the defined doses. The substance is tested using a stepwise procedure, each step using three animals of a single sex. Absence or presence of compound-related mortality of the animals dosed at one step will determine the next step, i.e.

− no further testing is needed

− dosing of three additional animals, with the same dose

− dosing of three additional animals at the next higher or the next lower dose level. The method will enable a judgment with respect to classifying the test substance to one of a series of toxicity classes.

Methodology:

Selection of Animal Species

The preferred rodent species is the Wister albino rat, although other rodent species may be used. Healthy young adult animals are commonly used laboratory strains should be employed. Females should be nulliparous and non-pregnant. Each animal, at the commencement of its dosing, should be between 6 to 8 weeks old and the weight (150-200gm) should fall in an interval within±20 % of the mean weight of any previously dosed animals.

Housing and Feeding Conditions

The temperature in the experimental animal room should be 22ºC ± 3ºC. Although the relative humidity should be at least 30% and preferably not exceed 70% other than during room cleaning the aim should be 50-60%. Lighting should be artificial, the sequence being 12 hours light, 12 hours dark. For feeding, conventional laboratory diets may be used with an unlimited supply of drinking water. Animals may be group-caged by dose, but the number of animals per cage must not interfere with clear observations of each animal.

Preparation of animals:

The animals are randomly selected, marked to permit individual identification, and kept in their cages for at least 7 days prior to dosing to allow for acclimatization to the laboratory conditions

Test Animals and Test Conditions:

Sexually mature Female Wistar albino rats (150-200gm) were obtained from TANUVAS, Madhavaram, and Chennai. All the animals were kept under standard environmental condition (22±3 ° C). The animals had free access to water and standard pellet diet (Saimeera foods, Bangalore).

Preparation of animals:

The animals are randomly selected, marked to permit individual identification, and kept in their cages for at least 7 days prior to dosing to allow for acclimatization to the laboratory conditions

Preparation for Acute Toxicity Studies

Rats were deprived of food overnight (but not water 16-18 h) prior to administration of the, ***KALINGATHI ENNAI***

The principles of laboratory animal care were followed and the Institutional Animal Ethical Committee approved the use of the animals and the study design

IAEC No: XLVIII/02/CLBMCP/2017

Test Substance	: **KALINGATHI ENNAI**
Animal Source	: Kings institute, Chennai.
Animals	: Wister Albino Rats (Female-3+3)
Age	**:** >6 weeks
Body Weight on Day 0	**:**150-180 gm.
Acclimatization	**:** Seven days prior to dosing.
Veterinary examination	**:** Prior and at the end of the acclimatization period.
Identification of animals	**:** By cage number, animal number and individual marking by using Picric acid.
Numberofanimals	: 3 Female/group,
Routeofadministration	: Oral
Diet	**:** Pelletfeed supplied by Saimeera foods PvtLtd,Bangalore

Water	**:** Aqua guard portable water in polypropylene bottles.
Housing & Environment	**:** The animals were housed in Polypropylene cages provided with bedding of husk.
Housing temperature	**:** between 22ºC ±3ºC.
Relative humidity	**:** between 30% and 70%,
Air changes	**:** 10 to 15 per hour and
Dark and light cycle	**:** 12**:**12 hours.
Duration of the study	**:** 14 Days

Administration of Doses:

KALINGATHI ENNAI was administered to the groups of wistar albino rats in a single oral dose by gavage using a feeding needle. The control group received an equal volume of the vehicle. Animals were fasted 12 hours prior to dosing. Following the period of fasting, the animals were weighed and then the test substance was administered. Three Female animals are used for each group. The dose level of 20, 100 and 200 mg/kg body weight was administered stepwise. After the substance has been administered, food was withheld for a further 3-4 hours. The principle of laboratory animal care was followed. Observations were made and recorded systematically and continuously as per the guideline after substance administration. The visual observations included skin changes, mobility, aggressively, sensitivity to sound and pain, as well as respiratory movements. Finally, the number of survivors was noted after 24 hrs and these animals were then monitored for a further 14 days and observations made daily. The toxicological effect was assessed on the basis of mortality.

Observations:

Animals are observed individually after dosing at least once during the first 30 minutes, periodically during the first 24 hours, with special attention given during the first 4 hours, and daily thereafter, for a total of 14 days, except where they need to be removed from the study and humanely killed for animal welfare reasons or are found dead. It should be determined by the toxic reactions, time of onset and length of recovery period, and may thus be extended when considered necessary. The times at which signs of toxicity appear and disappear are important, especially if there is a

tendency for toxic signs to be delayed. All observations are systematically recorded with individual records being maintained for each animal.

Observations include changes in skin and fur, eyes and mucous membranes, and also respiratory, circulatory, autonomic and central nervous systems, and somatomotor activity and behavior pattern. Attention was directed to observations of tremors, convulsions, salivation, diarrhoea, lethargy, sleep and coma. The principles and criteria summarized in the Humane Endpoints Guidance Document taken into consideration. Animals found in a moribund condition and animals showing severe pain or enduring signs of severe distress was humanly killed. When animals are killed for human reasons or found dead, the time of death was recorded.

Acute oral toxicity study of KALINGATHI ENNAI

Table 1: Dose finding experiment and its behavioral Signs of acute oral Toxicity

Observation done:

SL	Group CONTROL	Observation	SL	Group TEST GROUP	Observation
1	Body weight	Normal	1	Body weight	Normally increased
2	Assessments of posture	Normal	2	Assessments of posture	Normal
3	Signs of Convulsion Limb paralysis	Normal	3	Signs of Convulsion Limb paralysis	Absence of sign (-)
4	Body tone	Normal	4	Body tone	Normal
5	Lacrimation	Normal	5	Lacrimation	Absence
6	Salivation	Normal	6	Salivation	Absence

7	Change in skin color	No significant color change	7	Change in skin color	No significant color change
8	Piloerection	Normal	8	Piloerection	Normal
9	Defecation	Normal	9	Defecation	Normal
10	Sensitivity response	Normal	10	Sensitivity response	Normal
11	Locomotion	Normal	11	Locomotion	Normal
12	Muscle gripness	Normal	12	Muscle gripness	Normal
13	Rearing	Mild	13	Rearing	Mild
14	Urination	Normal	14	Urination	Normal

Behaviour:

The animals will be observed closely for behaviour in the first four hours which includes abnormal gait, aggressiveness, exophthalmos, ptosis, akinesia, catalepsy, convolusion, excitation, head twitches, lacrimation, loss of corneal reflex, loss of traction, piloerection reactivity of touch, salivation, scratching, sedation, chewing, head movements, sniffing, straub, tremor and writhes, diarrhea, leathery, sleep and coma.

Body Weight:

Individual weight of animals was determined before the test substance was administered and weights will be recorded at day 1, 7, and 14 of the study. Weight changes were calculated and recorded. At the end of the test, surviving animals were weighed and humanly killed.

Food and water Consumption:

Food and water consumed per animal was calculated for control and the treated dose groups.

Mortality:

Animals were observed for mortality throughout the entire period.

Results:

All data were summarized in tabular form, (Table-1-4) showing for each test group the number of animals used, the number of animals displaying signs of toxicity, the number of animals found dead during the test, description of toxic symptoms, weight changes, food and water intake.

No of animals in each group:3

Table 2 (Observational study Results)

No	Dose mg/kg	1	2	3	4	5	6	7	8	9	10	11	12	13	14	15	16	17	18	19	20
1.	**Control**	+	-	-	+	-	+	-	-	-	-	-	-	-	-	-	-	-	-	-	-
2.	**2000 mg/kg**	+	-	-	+	-	+	-	-	-	-	-	-	-	-	-	-	-	-	-	-

1..Alertness 2. Aggressiveness 3. Pile erection 4. Grooming 5. Gripping 6. Touch Response 7. Decreased Motor Activity 8.Tremors 9.Convulsions 10. Muscle Spasm 11. Catatonia 12. Muscle relaxant 13. Hypnosis 14.Analgesia 15.Lacrimation 16.Exophthalmos 17.Diarrhea 18. Writhing
19. Respiration 20. Mortality.

(+ Present, - Absent)

Table 3(Body weight Observation)

DOSE	DAYS		
	1	7	14
CONTROL	176.21± 3.22	177.2± 4.27	179.2 ± 4.82
2000 mg/kg	172.5± 3.18	174.2± 3.26	175.4 ± 3.27
P value (p)*	NS	NS	NS

Table 4 (Water intake (ml/day) of Wistar albino rats group exposed to (*KALINGATHI ENNAI):*

DOSE	DAYS		
	1	6	14
CONTROL	38.7 ± 2.74	32.9± 4.33	33.4± 4.13
2000 mg/kg	32.4±1.34	33.5±1.11	35. 9± 4.19
P value (p)*	NS	NS	NS

N.S- Not Significant,**($p > 0.01$), *($p > 0.05$), n = 10 values are mean ± S.D (One way ANOVA followed by Dunnett's test)

Table 5: Food intake (gm/day) of Wistar albino rats group exposed to KALINGATHI ENNAI

DOSE	DAYS		
	1	7	14
CONTROL	32.56±2.16	32.92±3.26	30.92±3.26
2000 mg/kg	34.12±8.64	34.31±1.22	35.22±2.24
P value (p)*	NS	NS	NS

REPEATED DOSE 28-DAY ORAL TOXICITY STUDY OF KALINGATHI ENNAI

Test Substance : ***KALINGATHI ENNAI***

Animal Source : Kings institute, Chennai.

Animals : Wister Albino Rats (Male -24, and Female-24)

Age **:** >6 weeks

Body Weight **:** 160-180 gm.

Acclimatization **:** Seven days prior to dose.

Veterinary examination **:** Prior and at the end of the acclimatization period.

Identification of animals **:** By cage number, animal number and individual marking by using Picric acid

Diet **:** Pellet feed supplied by Saimeera foods Pvt Ltd, Bangalore

Water **:** Aqua guard portable water in polypropylene bottles.

Housing & Environment **:** The animals were housed in Polypropylene cages provided with bedding of husk.

Housing temperature **:** between 22ºC $\pm$3ºC.

Relative humidity **:** between 30% and 70%,

Air changes **:** 10 to 15 per hour

Dark and light cycle **:** 12**:**12 hours.

Duration of the study **: 28 Days.**

Table 5

Groups	No of Rats
Group I Vehicle control (Normal Saline)	12(6male,6 female)
Group II KALINGATHI ENNAI20 mg/kg	12 (6male,6 female)
Group III KALINGATHI ENNAI100 mg/kg	12 (6male,6female)
Group IV KALINGATHI ENNAI200 mg/kg	12(6male,6female)

Methodology

Randomization, Numbering and Grouping of Animals:

48 Wistar Albino Rats (24M + 24F) were selected and divided into 4 groups. Each group consist of 12 animals (Male -6, and Female-6). First group treated as a control and other three group were treated with test drug (low, mid, high) for 28 days. Animals were allowed acclimatization period of 7 days to laboratory conditions prior to the initiation of treatment. Each animal was marked with picric acid. The females were nulliparous and non-pregnant.

Justification for Dose Selection:

As per OECD guideline three dose levels were selected for the study. They are low dose (20 mg/kg), mid dose dose (100 mg/kg), high dose (200 mg/kg). X is calculated by multiplying the dose (2000mg/kg) i.e**X low dose is 20 mg/kg/animal, 5X mid dose is 100 mg/kg, 10X high dose is 200 mg/kg.**

Preparation and Administration of Dose:

KALINGATHI ENNAI was administered to animals at the dose levels of 20, 100 and 200 mg/kg. The test substance suspensions were freshly prepared every two days once for 28 days. The control animals were administered vehicle only. The drug was administered orally by using oral gavage once daily for 28 consecutive days.

Observations:

Experimental animals were kept under observation throughout the course of study for the following:

Body Weight:

Weight of each rat was recorded on day 0, at weekly intervals throughout the course of study.

Food and water Consumption:

Food and water consumed per animal was calculated for control and the treated dose groups.

Clinical signs:

All animals were observed daily for clinical signs. The time of onset, intensity and duration of these symptoms, if any, were recorded.

Mortality:

All animals were observed twice daily for mortality during entire course of study.

Necropsy:

All the animals were sacrificed by excessive anesthesia on day 29. Necropsy of all animals was carried out.

Laboratory Investigations:

Following laboratory investigations were carried out on day 29 in animals fasted over-night. Blood samples were collected from orbital sinus using sodium heparin (200IU/ml) for Bio chemistry and potassium EDTA (1.5 mg/ml) for Hematology as anticoagulant. Blood samples were centrifuged at 3000 r.p.m. for 10 minutes.

Haematological Investigations:

Haematological parameters were determined using Haematology analyzer.

Biochemical Investigations:

Biochemical parameters were determined using auto-analyzer.

Histopathology:

Control and highest dose group animals will be initially subjected to histopathological investigations. If any abnormality found in the highest dose group than the low, then the mid dose group will also be examined. Organs will be collected from all animals and preserved in 10% buffered neutral formalin for 24 h and washed in running water for 24 h. The organ sliced 5 or 6µm sections and were dehydrated in an auto technicon and then cleared in benzene to remove absolute alcohol. Embedding was done by passing the cleared samples through three cups containing molten paraffin at 50°C and then in a cubical block of paraffin made by the "L" moulds. It was followed by microtome and the slides were stained with Haematoxylin-eosin red.

Statistical analysis:

Findings such as body weight changes, water and food consumption,hematology and blood chemistry were subjected to One-way ANOVA followed by dunnet t test using a computer software programme – Graph pad version 5.0 .All data were summarized in tabular form, (Table-6 to 12)

RESULTS

Repeated Dose 28- day oral toxic study of KALINGATHI ENNAI

Table 6: Body weight of wistar albino rats group exposed to KALINGATHI ENNAI

DOSE	DAYS				
	1	7	14	21	28
CONTROL	165.6± 2.76	166.4 ± 3.42	167.7 ± 3.26	169.2 ± 3.73	170.7 ± 1.31
LOW DOSE	162.2 ± 4.12	162.7 ± 2.64	163.9± 1.\ 1	164.9 ± 1.66	164.42± 2.76
MID DOSE	167.6± 1.24	167.9 ± 4.74	169.4 ± 8.92	169.1 ± 6.36	170.7 ± 9.12
HIGH DOSE	174.4± 3.74	174.6 ± 6.32	175.6 ± 2.86	176.1± 8.82	175.32 ± 2.42
P value (p)*	NS	NS	NS	NS	NS

NS- Not Significant, **(p > 0.01),*(p >0.05), n = 10 values are mean ± S.D (One way ANOVA followed by Dunnett's test)

Table 7: Water intake (ml/day) of Wistar albino rats group exposed to *KALINGATHI ENNAI*

DOSE	DAYS				
	1	6	14	21	28
CONTROL	31.5 ± 8.95	32.0 ±6.23	28.5±6.23	29.12±8.19	31.5±3.96
LOW DOSE	29.5±3.31	29.9±6.62	31.7±4.02	32.2±4.29	34.9±3.13
MID DOSE	30.7±3.93	30.3±3.11	30.1±2.83	31.4±2.11	31.4±1.14
HIGHDOSE	31.1±1.12	31.2±2.43	32.7±2.53	33.2±1.89	34.4±2.45
P value (p)*	NS	NS	NS	NS	NS

N.S- Not Significant, **(p > 0.01), *(p >0.05), n = 10 values are mean ± S.D (One way ANOVA followed by Dunnett's test)

Table 8: Food intake (gm/day) of Wistar albino rats group exposed to KALINGATHI ENNAI

DOSE	DAYS				
	1	7	14	21	28
CONTROL	37.12 ±5.37	38.5±3.22	39.5±3.37	38.5±3.37	37.12±3.12
LOW DOSE	33.7±2.12	35.3±1.42	35.9±1.68	36.4±2.62	35.9±8.42
MID DOSE	34.2±3.64	35.9±3.64	36.2±6.15	37.4±2.18	35.2±2.64
HIGH DOSE	35.2±2.14	35.2±2.18	36.6±2.14	37.2±4.28	37.2±2.18
P value (p)*	NS	NS	NS	NS	NS

N.S- Not Significant, **(p > 0.01), *(p >0.05), n = 10 values are mean ± S.D (One way ANOVA followed by Dunnett's test

Table 9: Haematological parameters of Wistar albino rats group exposed to KALINGATHI ENNAI

Category	Control	Low dose	Mid dose	High dose	P value (p)*
Haemoglobin(g/dl)	13.8±1.88	12.98±1.28	13.01±1.26	14.18±3.96	N.S
Total WBC (×10^{3}l)	11.91±2.59	12.25±3.53	12.18±3.61	12.96±3.47	N.S
Neutrophils(%)	31.60±1.06	34.23±2.54	34.91±1.36	33.40±2.80	N.S
lymphocyte (%)	68.32±2.48	70.22±3.42	71.48±2.66	71.20±3.96	N.S
Monocyte (%)	0.80±0.17	0.81±0.12	0.84±0.11	0.95±0.16	N.S
Eosinohil(%)	0.62±0.09	0.19±0.12	0.78±0.06	0.42±0.04	N.S
Platelets cells10^3/µl	683.17±8.76	698.71±8.16	705.18±4.0	712.16±4.64	N.S
Total RBC 10^6/µl	7.96±0.12	6.82±1.87	6.92±0.59	6.18±0.72	N.S
PCV%	36.75±0.6	36.35±1.53	38.2±1.18	36.82±2.14	N.S
MCHC g/dL	32.6±2.23	34.19±1.19	35.18±1.92	34.13±1.94	N.S
MCV fL(µm^3)	48.15±3.64	48.20±1.24	49.28±1.24	49.99±1.84	N.S

N.S- Not Significant, **($p > 0.01$), *($p > 0.05$), n = 10 values are mean ± S.D (One way ANOVA followed by Dunnett's test)

Table 10: Biochemical Parameters of Wistar albino rats group exposed to KALINGATHI ENNAI

BIOCHEMICAL PARAMETERS	CONTROL	LOW DOSE	MID DOSE	HIGH DOSE	P Value (p)*
GLUCOSE (R) (mg/dl)	76.45±13.4	76.16±8.54	79.64±9.20	77.42±11.6	N.S
T.CHOLOSTEROL(mg/dl)	115.26±1.83	112.45±1.13	112.42±1.98	115.22±1.83	N.S
TRIGLY(mg/dl)	46.35±1.48	45.32±1.48	45.58±1.26	46.66±1.45	N.S
LDL	72.81±2.13	70.14±2.34	71.8±2.94	72.64±6.12	NS
VLDL	15.2±2.44	14.42±4.63	14.44±6.64	14.94±5.14	NS
HDL	26.66±6.88	27.96±2.34	27.88±5. 66	29.78±6.22	NS
Ratio1(T.CHO/HDL)	4.42±2.44	4.36±1.44	4.84±2.44	4.86±1.92	NS
Ratio 2(LDL/HDL)	2.83±4.22	3.02±1.52	2.96±4.80	2.86±3.82	NS
Albumin(g/dL)	3.63±0.17	3.13±1.12	3.10±1.92	2.94±3.86	NS

NS- Not Significant,**(p > 0.01), * (p >0.05), n = 10 values are mean ± S.D (One way ANOVA followed by Dunnett's test)

Table 11: Renal function test of ofWistar albino rats group exposed to KALINGATHI ENNAI

PARAMETERS	CONTROL	LOW DOSE	MID DOSE	HIGH DOSE	P Value (p)*
UREA (mg/dl)	12.31±0.99	12.91±1.86	13.16±1.98	13.18±3.92	N.S
CREATININE(mg/dl)	0.22±0.08	0.16±1.16	0.12±0.14	0.18±1.22	N.S
BUN(mg/dL)	14.02±0.10	14.80±1.20	14.66±0.44	15.10±2.32	NS
URIC ACID(mg/dl)	5.12±0.35	5.25±1.43	5.02±1.35	5.18±1.08	NS

NS- Not Significant, **(p > 0.01), * (p >0.05) , n = 10 values are mean ± S.D (One way ANOVA followed by Dunnett's test

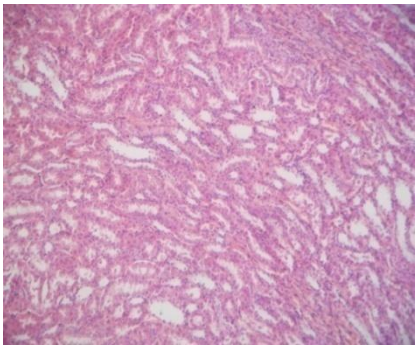
Table 12: Liver Function Test of ofWistar albino rats group exposed to KALINGATHI ENNAI

PARAMETERS	CONTROL	LOW DOSE	MID DOSE	HIGH DOSE	P Value (p)*
T BILIRUBIN(mg/dl).	0.48±0.07	0.43±1.26	0.64±1.28	0.68±1.25	N.S
SGOT/AST(U/L)	79.95±1.39	77.15±1.31	78.71±1.83	80.35±3.03	N.S
SGPT/ALT(U/L)	31.23±1.28	31.81±3.52	30.14±3.18	31.9±1.88	N.S
ALP(U/L)	143.25±8.70	141.9±8.17	142.16±4.10	144.33±4.25	NS
T.PROTEIN(g/dL)	5.32±0.38	5.28±0.34	5.21±1.33	5.13±1.06	N.S

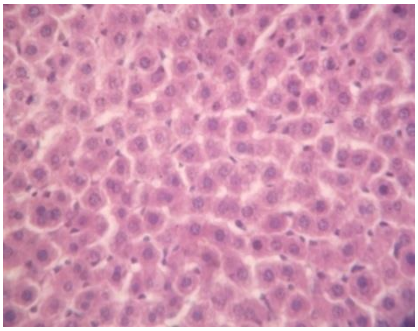
NS- Not Significant, **(p > 0.01), * (p >0.05), n = 10 values are mean ± S.D (One way ANOVA followed by Dunnett's test)

HISTO PATHOLOGY

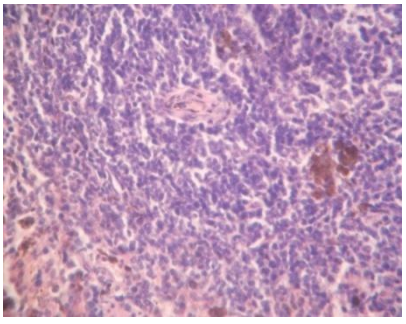
CONTROL GROUP



Kidney

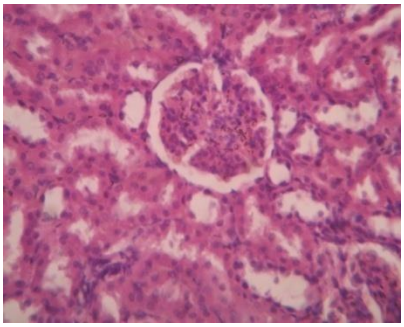


Liver

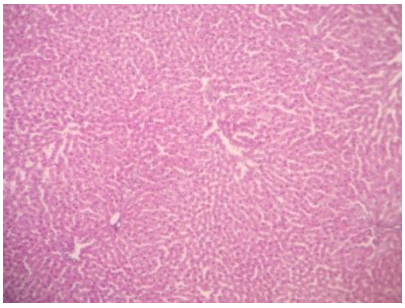


Spleen

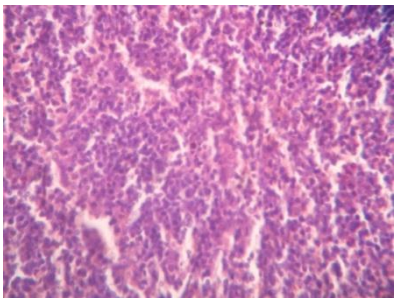
TEST GROUP (HIGH DOSE)



Kidney



Liver



Spleen

PHARMACOLOGICAL ACTIVITY
OVULATION INDUCING ACTIVITY OF KALINGATHI ENNAI

ANIMAL PROCUREMENT AND MAINTENANCE:

Female Wistar albino rats weighing about 150-200g were purchased from Kings Institute of Preventive medicine animal house, Chennai, India. Animal ethical guidelines of CPCSEA, Ministry of Animal Husbandry and Welfare, Govt. of India were strictly followed for the care and maintenance of procured animals. The animals were fed on standard rodent pellet and RO Water was provided ad libitum. The animals were kept for overnight fasting before experimentation.

Method

Before starting drug treatment, the reproductive cycles of the rats were synchronized by the following method. 100µg estradiol dissolved in 2 ml olive oil was injected subcutaneously. All rats after a 24 hr period, received intramuscular injections of 50 µg progesterone dissolved in olive oil. After few hours, vaginal smears were obtained by vaginal lavage to monitor ovulation and oestrous cycle. Vaginal smears were prepared by washing vaginal opening with 0.9% w/v of sodium chloride with a glass dropper and placed in a clean glass slide and viewed under light microscope at 40X magnification. Examination of vaginal smears showed that all the animals were in the oestrous stage.

All the animals were weighed daily after drug administration for 10 days. The suitable sensitive rats were divided into four groups of six each as follows

Experimental design

- Group I Normal Control animals 1ml/kg of CMC solution.
- Group II rats were administered Kalingathi ennai100mg/kg for 10days,
- Group III rats were administered Kalingathi ennai 200mg/kg for 10 days
- Group IV received Clomiphene 10mg/kg and served as standard. All the drugs were given orally.

After that 2ml of blood was collected by retro orbital puncture. Blood samples were centrifuged for 15 minutes at 4000 rpm and the separated serum samples were frozen at -20°C and kept for later estimation of LH, FSH and Estradiol by ELISA method.

4.4.2 Hormonal assay

Biochemical assay

The method employed was Microwell Enzyme Linked Immunosorbent Assay (ELISA) using analytical grade reagents.

Estimation of serum luteinizing hormone (LH)

The method employed was Microwell immunoassay (ELISA) using analytical grade reagents. 0.050ml of the serum was pipetted into the assigned wells. 0.001ml of LH-Enzyme reagent was added to all the wells. The microplate was swirled for 20-30 seconds and covered, this mixture was allowed to incubate for 60 minutes at room temperature. After which, the contents were discarded by decantation. 350µl of wash buffer was added and decanted for 3 times. 100µl of working substrate solution was added to all the wells and was allowed to incubate for fifteen minutes. 50µl of stop solution was added to all the wells and gently mixed for 20 seconds. The optical density was read at 450nm in a microplate reader within 30mins. The mean absorbance values for each set of standards, controls, and test samples were calculated and a standard curve was constructed by plotting a mean absorbance obtained from each of the reference standard against its concentration from the standard curve.

Estimation of serum follicle stimulating hormone (FSH)

The method employed was Microwell immunoassay (ELISA) using analytical grade reagents. 0.050ml of the serum was pipetted into the assigned wells. 0.001ml of FSH-Enzyme reagent was added to all the wells. The microplate was swirled for 20-30 seconds and covered, this mixture was allowed to incubate for 60 minutes at room temperature. After which, the contents were discarded by decantation. 350µl of wash buffer was added and decanted for 3 times. 100µl of working substrate solution was added to all the wells and was allowed to incubate for fifteen minutes. 50µl of stop solution was added to all the wells and gently mixed for 20 seconds. The optical density was read at 450nm in a microplate reader within 30mins.The mean absorbance values for each set of standards, controls, and test samples were calculated and a standard curve was constructed by plotting a mean absorbance obtained from each of the reference standard against its concentration from the standard curve

Determination of serum progesterone levels

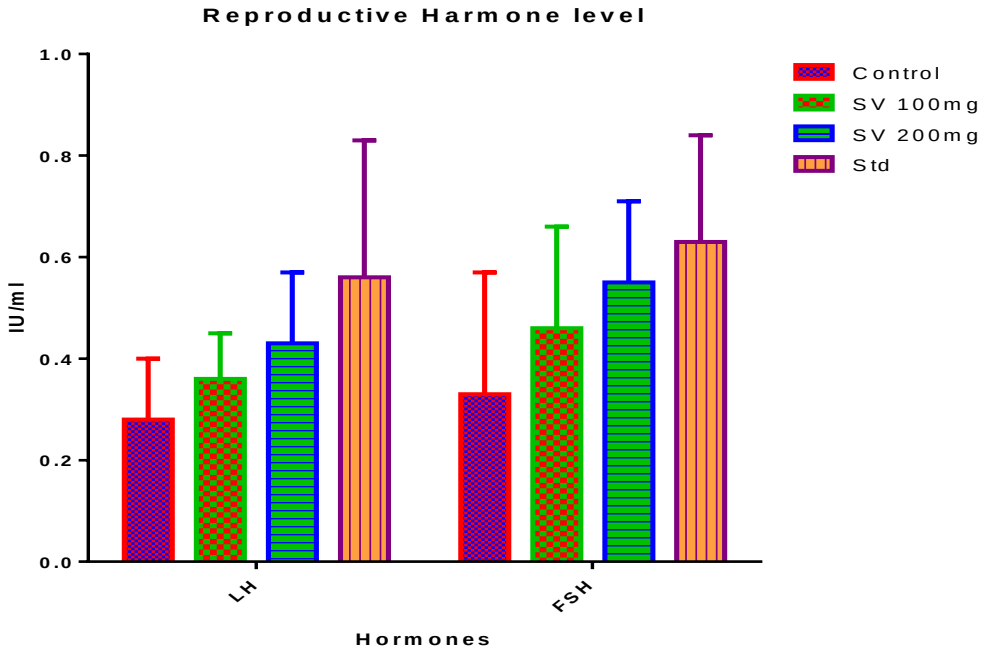
The method employed was Microwell immunoassay (ELISA) using analytical grade reagents. 0.025ml of the serum was pipetted into the assigned wells. 0.050ml of progesterone Enzyme reagent was added to all the wells. The microplate was swirled for 20 seconds to mix, 0.050ml progesterone biotin reagent was added to all the wells, the mixture was swirled for 20 seconds to mix and covered, this mixture was allowed to incubate for 60 minutes at room temperature. After which, the contents were discarded by decantation. 350µl of wash buffer was added and decanted for 3 times. 100µl of working substrate solution was added to all the wells and was allowed to incubate for twenty minutes. 50µl of stop solution was added to all the wells and gently mixed for 20 seconds. The optical density was read at 450nm in a microplate reader within 30mins. The mean absorbance values for each set of standards, controls, and test samples were calculated and a standard curve was constructed by plotting a mean absorbance obtained from each of the reference standard against its concentration from the standard curve.

Determination of serum Estradiol levels

The method employed was Microwell immunoassay (ELISA) using analytical grade reagents. 0.025ml of the serum reference was pipetted into the assigned wells. 0.050ml of Estradiol Biotin reagent was added to all the wells. The microplate was swirled for 20 seconds to mix, the mixture was incubated at room temperature for 30mins,0.050ml Estradiol enzyme reagent was added to all the wells , the mixture was swirled for 20 seconds to mix and covered, this mixture was allowed to incubate for 90 minutes at room temperature. After which, the contents were discarded by decantation. 350µl of wash buffer was added and decanted for 3 times. 100µl of working substrate solution was added to all the wells and was allowed to incubate for twenty minutes. 50µl of stop solution was added to all the wells and gently mixed for 20 seconds. The optical density was read at 450nm in a microplate reader within 30mins. The mean absorbance values for each set of standards, controls, and test samples were calculated and a standard curve was constructed by plotting a mean absorbance obtained from each of the reference standard against its concentration from the standard curve

Effect of Kalingathi ennai on Serum Concentration of reproductive hormones of female Wister albino rat

S. No	Group	Treatment and dose	LH (IU/ml)	FSH (IU/ml)	Estrodial (pg/ml)	Progesterone (pg/ml)
1.	Normal	2ml/kg 2% CMC	0.28±0.12	0.33±0.24	54.10±3.5	9.03±1.65
2.	Low dose	KGE 100 mg /kg	0.36±0.09	0.46±0.20	38.32± 2.6	6.6±1.14
3.	High dose	KGE 200 mg /kg	0.43±0.14	0.55± 0.16	32.68± 2.1	6.4±0.46
4.	Standard	Clomiphene 10mg/kg	0.56±0.27	0.63± 0.21	27.17± 1.8	5.9±0.86


Reproductive Harmone level
1.0
0.8
0.6
0.4
0.2
0.0
IU/ml
Control
SV 100mg
SV 200mg
Std
LH
FSH
Hormones

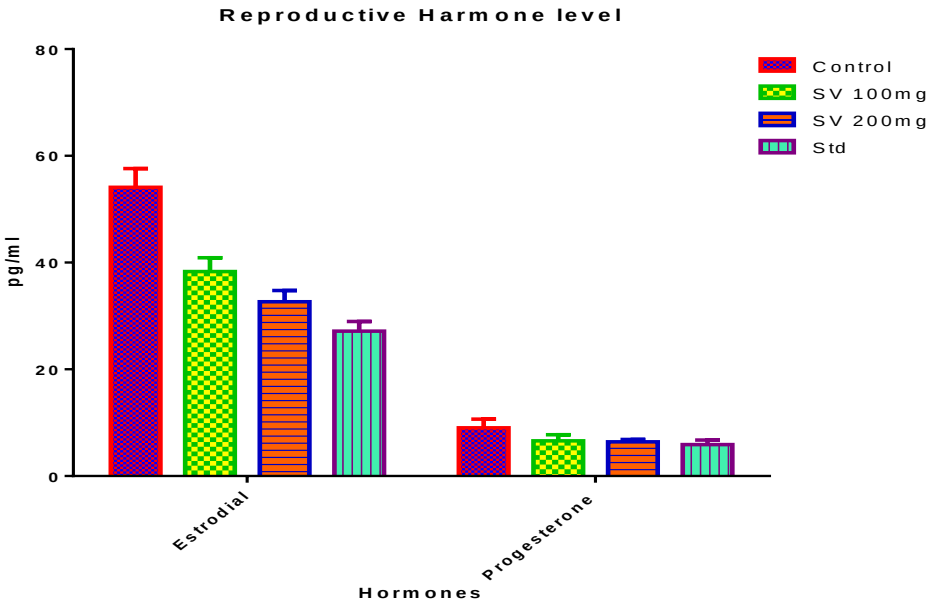

Reproductive Harmone level
80
60
40
20
0
pg/ml
Control
SV 100mg
SV 200mg
Std
Estrodial
Progesterone
Hormones

Table 1— Physicochemical analysis of samples of kalingathi ennai

[Values are mean of three determinations ±SEM]

Parameters	Total ash	Values
Ash value	Water soluble ash	8.75±0.011
	Acid insoluble ash	0.85±0.011
Extractive value	Water soluble extractive value	7.20±0.310
Loss on drying	Loss on drying at 70°C	8.20±0.240
Colour	Yellow	
pH Analysis		6.540

SEM- singularity **expansion** method

Project Report

Project ID	NRS/AS/0153/06/2018
Name and Address of the Researcher	Dr.S.Brundha Govt.Siddha Medical College, Chennai,Tamilnadu, India
Parameter Requested by the Customer for Analysis	Phytochemical Analysis
Sample Received	Post
Sample –ID	Kalingathi ennai- KE

PHYTOCHEMICAL ANALYSIS

Test for alkaloids:

Mayer's Test: To the test sample, 2ml of mayer's reagent was added, a dull white precipitate revealed the presence of alkaloids.

Test for coumarins:

To the test sample, 1 ml of 10% sodium hydroxide was added. The presence of coumarins is indicated by the formation of yellow color.

Test for saponins:

To the test sample, 5 ml of water was added and the tube was shaken vigorously. Copious lather formation indicates the presence of Saponins.

Test for tannins:

To the test sample, ferric chloride was added, formation of a dark blue or greenish black color showed the presence of tannins.

Test for glycosides- Borntrager's Test

Test drug is hydrolysed with concentrated hydrochloric acid for 2 hours on a water bath, filtered and the hydrolysate is subjected to the following tests. To 2 ml of filtered hydrolysate, 3 ml of choloroform is added and shaken, choloroform layer is separated and 10% ammomia solution is added to it. Pink colour indicates presence of glycosides.

Test for flavonoids:

To the test sample about 5 ml of dilute ammonia solution were been added followed by addition of few drops of conc. Sulfuric acid. Appearance of yellow color indicates the presence of Flavonoids.

Test for phenols:

Lead acetate test: To the test sample; 3 ml of 10% lead acetate solution was added. A bulky white precipitate indicated the presence of phenolic compounds.

Test for steroids:

To the test sample , 2ml of chloroform was added with few drops of conc. Sulphuric acid (3ml), and shaken well. The upper layer in the test tube was turns into red and sulphuric acid layer showed yellow with green fluorescence. It showed the presence of steroids.

Triterpenoids

Liebermann–Burchard test: To the chloroform solution, few drops of acetic anhydride was added then mixed well. 1 ml concentrated sulphuric acid was added from the sides of the test tube, appearance of red ring indicates the presence of triterpenoids.

Test for Cyanins

A. Aanthocyanin:

To the test sample, 1 ml of 2N sodium hydroxide was added and heated for 5 min at 100°C. Formation of bluish green colour indicates the presence of anthocyanin.

Test for Carbohydrates - Benedict's test

To the test sample about 0.5 ml of Benedic's reagent is added. The mixture is heated on a boiling water bath for 2 minutes. A characteristic coloured precipitate indicates the presence of sugar.

Proteins (Biuret Test)

To extracts 1% solution of copper sulphate was added followed by 5% solution of sodium hydroxide, formation of violet purple colour indicates the presence of proteins.

Reference : Brain KR, Turner TD. The Practical Evaluation of Phytopharmaceuticals. Bristol: Wright Scientechnica; 1975:36-45

Noble research solutions
We Trust in Quality and Ethics

Noble Research Solutions

We Trust in Quality and Ethics

E-mail: nobleresearchsolutions@gmail.com
Contact: 9710437419, Admin: 044 - 42691289

Project ID	NRS/AS/0153/06/2018
Name and Address of the Researcher	Dr.S.Brundha Govt Siddha Medical College, Chennai Tamil Nadu, India
Parameter Requested for Analysis	Phytochemical Analysis
Sample Received	Post
Sample –ID	Kalingathi Ennai - KE
Description of the Sample	Solid
Method of Analysis	PLIM- Protocol – ASU Formulations
Analysis Type	Physicochemical Analysis
Date of Analysis	22/06/2018
Result of Analysis	Test and Analytical Reports Attached As Annexures

Test Report

S.NO	TEST	OBSERVATION
1	ALKALOIDS	-
2	FLAVANOIDS	-
3	GLYCOSIDES	+
4	STEROIDS	+
5	TRITERPENOIDS	+
6	COUMARIN	+
7	PHENOL	-
8	TANIN	-
9	PROTEIN	-

Noble Research Solutions
We Trust in Quality and Ethics
E-mail: nobleresearchsolutions@gmail.com
Contact: 9710437419, Admin: 044 - 42691289

10	SAPONINS	+
11	SUGAR	+
12	ANTHOCYANIN	-
13	BETACYANIN	+

Note: +-> Indicates Presence and - -> Indicates Absence of the Phytocomponents.

ANNEXURE-II

BIO-CHEMICAL ANALYSIS OF TRIAL MEDICINE

S.No	EXPERIMENT	OBSERVATION	INFERENCE
I	**TEST FOR ACID RADICALS**		
1a	**Test for Sulphate** 2 ml of the above prepared extractis taken in a test tube. To this add2ml of 4% Ammonium oxalatesolution.	Absence of White Precipitate	Absent
b	2ml of extract is added with 2mlof dilute hydrochloric acid untilthe effervescence ceases off. Then2ml barium chloride solution isadded.	Absence of White Precipitate	Absent
2	**Test for Chloride:** 2ml of extract is added with dilutenitric acid till the effervescenceceases. Then 2ml of silver nitratesolution is added.	Absence of white precipitate	Absent
3	**Test for Phosphate** 2ml of the extract is treated with 2 ml of Ammonium molybdate solution and 2ml of concentrated nitric acid.	Absence of yellow precipitate	Absent
4	**Test for Carbonate:** 2ml of the extract is treated with 2ml of magnesium sulphate solution.	Absence of white precipitate	Absent
5	**Test for Sulphide:** 1 gm of the substance is treated with 2ml of concentrated Hydrochloric acid	Absence of rotten egg smelling	Absent

6	**Test for Nitrate:** 1gm of the substance is heated with copper turnings and concentrated sulphuric acid and viewed the test tube vertically down.	Absence of reddish brown gas.	Absent
7a	**Test for Fluoride and oxalate** 2ml of the extract is added with 2ml of dilute acetic acid and 2ml of calcium chloride solution and heated.	White precipitate absent	Absent
b	5 drops of clear solution is added with 2ml of dilute sulphuric acid and slightly warmed to this, 1 ml of dilute potassium permanganate solution is added.	Absence of KMNO4 solution Discolourisation	Absent
8	**Test for Nitrite** 3 drops of the extract is placed on a filter paper. On that, 2 drops a Acetic Acid and 2 drops of Benzidine solution is placed.	Absence of yellowish red colour	Absent
9	**Test for Borate** 2 pinches of the substance is made into paste by using Sulphuric acid and Alcohol (95%) and introduced into the blue flame.	Absence of Green tinged flame	Absent
II	**TEST FOR BASIC RADICALS**		
10	**Test for lead**	Absence of Yellow	Absent

	2 ml of the extract is added with 2 ml of Potassium iodide solution.	precipitate	
11a	**Test for Copper** One pinch of substance is made into paste with concentrated Hydrochloric acid in a watch glass and introduced into the non luminous part of the flame.	Absence of Bluish green coloured flame.	Absent
b	2ml of the extract is added with excess of Ammonia solution	Aresence of deep blue	Absent
12	**Test for Aluminium** To the 2 ml of extract. Sodium Hydroxide solution is added in drops to excess.	Absence of White Precipitate.	Absent
13a	**Test for Iron** To the 2 ml of extract, 2 ml of Ammonium Thiocyanate Solution is added.	Absence of Blood red colour	Absent
b	To the 2 ml of extract, 2 ml of Ammonium Thiocyanate solution and 2 ml of concentrated HNO_3 isadded.	Absence of blood red colour.	Absent
14	**Test for Zinc** To the 2 ml of extract Sodium Hydroxide solution is added in drops to excess.	Absence of White precipitate.	Absent
15	**Test for Calcium** 2 ml of the extract is added with 2 ml of 4% Ammonium Oxalate solution.	Absence of White precipitate.	Absent

16	**Test for Magnesium** 2ml of extract, Sodium Hydroxide solution is added in drops to excess.	Absence of White precipitate.	Absent
17	**Test for Ammonium** 2 ml of extract few ml of Nessler's Reagent and excess of Sodium Hydroxide solution are added.	Absence of Reddish brown precipitate	Absent
18	**Test for Potassium** A pinch of substance is treated with 2 ml of Sodium Nitrite solution and then treated with 2 ml of Cobal Nitrate in 30% glacial Acetic acid.	Absence of Yellow precipitate	Absent
19	**Test for Sodium** 2 pinches of the substance is made into paste by using Hydrochloric acid and introduced into the blue flame	Absence of Yellow colour flame	Absent
20	**Test for Mercury** 2 ml of the extract is treated with 2 ml of Sodium Hydroxide solution.	Absence of yellow precipitate	Absent
21	**Test for Arsenic** 2 ml of extract is treated with 2 ml of silver Nitrate solution	Absence of Yellow precipitate	Absent
22	**Test for Starch** 2ml of extract is treated with weak iodine solution	Absence of Blue colour	Absent
23	**Test of reducing Sugar** 5ml of Benedicts qualitative	Presence of Green colour	Present

	solution is taken in a test tube and allowed to boil for 2 minutes and added 10 drops of the extract and again boiled for 2 minutes. The colour changes are noted.		
24	**Test of the alkaliods** 2ml of the extract is treated with 2ml of potassium Iodide solution.	Absence of Red colour	Absent
25	**Test of the proteins** 2ml of the extract is treated with 2ml of 5% NaOH ,mix well and add 2 drops of copper sulphate solution.	Absence of Violet colour	Absent

RESULTS:

The given sample (Kalingathi ennai) contains Reducing sugar.

GOVERNMENT SIDDHA MEDICAL COLLEGE
Arumbakkam, Chennai-106

Communication Of The Decision Of Institutional Ethics Committee (IEC)

IEC No: GSMC-CH-ME-5/002/2016

Protocol title:

AN OPEN NON-RANDOMIZED CLINICAL TRIAL OF KALINGATHI ENNAI IN SOOTHAGA VAAYU (POLY CYSTIC OVARIAN SYNDROME).

Principal Investigator: Dr. S. BRUNDA

Name & Address of Institution:

Government Siddha Medical College,

Arumbakkam, Chennai-106

☑ New Review ☐ Revised Review ☐ Expedited Review

Date of review (DD/MM/YY): 05-04-2016

Date of Previous Review, If Revised Application:

Decision of the IEC

☑ Recommended ☐ Recommended with suggestions

☐ Revision ☐ Rejected

Suggestions / Reasons / Remarks:

1) Outcome should be changed (Regulation of Menstruation with regular cycle)

Recommended for a period of 1 year
from date of completion of preclinical studies :

Please Note:

- Inform IEC immediately in case of any adverse events/serious drug reaction.
- Seek IECapproval in case of any change in the study procedure, site and investigator
- This approval is valid only for period mentioned above
- IEC member have the right to review the trial with prior intimation.

5/4/16

Dr.P.Jeyaprakashnarayanan, M.D(s)
Chairman

Dr.K.Kanakavalli, M.D(s)
Member Secretary

INSTITUTIONAL ETHICS COMMITTEE

Date : 05/04/2016.
Sub : IEC review of research proposals.
Ref : Your letter dated

MEMBERS	PARTICIPATION	SIGNATURE
Dr.P.JEYAPRAKASH NARAYANAN, M.D(S)., Chairman	✓	
Dr.K.KANAKAVALLI, M.D(S)., Member secretary	✓	
Dr.P.SATHYA RAJESWARAN, M.D(S)., Clinician – Siddha	✓	
Dr.N.KABILAN, M.D(S)., Clinician – Siddha	✓	
Dr.R.VASUDEVAN, M.D(S)., PG.DIP (Clinical research), Msc (Medical sociology) Sociologist	✓	
Dr.L.MUKUNTHAN, M.B.B.S., DNB (Medicine)., Modern Medicine Specialist	✓	
Dr. JOSEPH MARIYA ADAIKKALAM,M.D(S)., Msc epidemiology., Social scientist	✓	
Dr.G.AADINATH REDDY, M.Pharm, Ph,D., Biomedical scientist	✓	05/04/16
Mr.B.PADMANABHA PILLAI Philosopher	✓	
Mrs. PREETHA SARAVANAN Public person	✓	05/04/16

5/4/16

Dr. P. Jeyaprakashnarayanan, M.D(s)
Chairman

Dr.K. Kanakavalli, M.D(s)
Member secretary

BIOSTATISTICAL ANALYSIS

CLINICAL PROGNOSIS

TREAMENT FOR SOOTHAGA VAAYU

The most popular non parametric statistical tool, namely, McNemar Test analysis has been employed to analyses the effectiveness with the help of a hypothesis.

S.No	Signs and Symptoms	Before Treatment	After Treatment
		n%	n%
1.	Irregular menstruation	40(100)	10(25)**
2.	Oligomenorrhoea	26(65)	2(5)**
3.	Dysmennorrhoea	20(50)	2(5)**
4.	Infertility	4(10)	2(5)*
5.	Hirsutism	6(15)	4(10)*
6.	Acanthosis nigricans	10(25)	8(20)*

McNemat test, C.I: 95%, *P<0.005; **P<0.001

Software: spss 17 version

Number of cases: 40

Inference:

Since the p value is significant in all signs and symptoms. So there is significant reducing of signs and symptoms among the patients for the treatment of Soothaga vaayu. Hence it is concluded that the treatment was effective and significant.

GOVERNMENT SIDDHA MEDICAL COLLEGE

ARIGNAR ANNA GOVERNMENT HOSPITAL OF INDIAN MEDICINE

CHENNAI – 600 106

CLINICAL STUDY ON **"KALINGATHI ENNAI"** IN THE TREATMENT OF

"SOOTHAGA VAAYU" (POLYCYSTIC OVARIAN SYNDROME)

INFORMED CONSENT FORM

"I have read the foregoing information. I have had the opportunity to ask questions about it and any questions I have asked have been answered to my satisfaction.

I consent voluntarily to participate in this study and understand that I have the right to withdraw from the study at any time without in any way it affecting my further medical care".

"I have received a copy of the information sheet/consent form".

Date:

Station:

Signature of participant:

Signature of the Guide: Signature of theInvestigator:

அரசினர் சித்த மருத்துவக் கல்லூரி சென்னை 106
அறிஞர் அண்ணா மருத்துவமனை சென்னை

சூதகவாயு நோய்க்கான சித்த மருந்தின் (கலிங்காதி எண்ணெய்) பரிகரிப்புத் திறனைக் கண்டறியும் மருத்துவ ஆய்விற்கான தகவல் படிவம் ஒப்புதல் படிவம்

ஆய்வாளரால் சான்றளிக்கப்பட்டது

நான் இந்த ஆய்வை குறித்த அனைத்து விபரங்களையும் நோயாளிக்கு புரியும் வகையில் எடுத்துரைத்தேன் என உறுதியளிக்கிறேன்

தேதி : கையொப்பம் :
இடம் : பெயர் :

நோயாளியின் ஒப்புதல்

என்னிடம் இந்த மருத்துவ ஆய்வின் காரணத்தையும், மருந்தின் தன்மை மற்றும் மருத்துவ வழிமுறை பற்றியும், தொடர்ந்து எனது உடல் இயக்கத்தை கண்காணிக்கவும் ,அதனை பாதுகாக்கவும் பயன்படும் மருத்துவ ஆய்வுக்கூட பரிசோதனைகள் பற்றி திருப்தி அளிக்கும் வகையில் ஆய்வு மருத்துவரால் விளக்கிக் கூறப்பட்டது.

நான் மருத்துவ ஆய்வின் போது ,காரணம் எதுவும் கூறாமல் ,எப்பொழுது வேண்டுமானாலும் இந்த ஆய்விலிருந்து என்னை விடுவித்து கொள்ளும் உரிமையை தெரிந்திருக்கின்றேன். நான் என்னுடைய சுதந்திரமாக தேர்வு செய்யும் உரிமையைக் கொண்டு சூதகவாயு நோய்க்கான கலிங்காதி எண்ணெய் மருந்தின் பரகரிப்புத் திறனைக் கண்டறியம் மருத்துவ ஆய்விற்கு என்னை உட்படுத்த ஒப்புதல் அளிக்கிறேன்.

தேதி : கையொப்பம் :
இடம் : பெயர் :

ஊறவுமுறை: சாட்சிக்காரர் கையொப்பம்

பெயர் :

தேதி :
இடம் :

CASE SHEET PROFORMA
GOVERNMENT SIDDHA MEDICAL COLLEGE
POST GRADUATE DEPARTMENT – MARUTHUVAM BRANCH
CHENNAI – 600 106.

CASE SHEET PROFORMA FOR SOOTHAGA VAAYU
(POLYCYSTIC OVARIAN SYNDROME – PCOS)

OP No / IP No	:	Nationality	: Indian
Ward No	:	Religion	:
Bed No	:	D.O.A	:
Name (In Block Letters)	:	D.O.D	:
Age	:	No of Days Treated	:
Sex	: Male/ Female		
Occupation	:	Diagnosis	:
Income	: /Month	Result	:
Permanent Address	:		

Temporary Address : Govt. Siddha Medical College,
Chennai – 600 106.

1. Complaint and duration :

2. History of present illness :

3. History of previous illness :

4. Personal history

Marital History :

Duration of married life :

Food :

Abortion :

5. Menstrual history :

Regularity of cycle :

Length of cycle (Days) :

Duration of flow (Days) :

Level of flow :

Abdominal pain :

LMP :

6. Occupational history :

7. Personal habits :

8. Family history :

GENERAL EXAMINATION:

Body built

Anaemia

Jaundice

Cyanosis

Clubbing

JVP

Tracheal deviation

Pedal oedema

Lymph adenopathy

VITAL SIGNS

Temperature

Pulse

Respiratory rate

Blood Pressure

Weight

Height

Hirsutism

Acanthosis nigricans

SIDDHA ASPECT

1. NILAM: 5

Kurinji

Mullai

Marutham

Neithal

Paalai

2. PARUVA KAALAM: 6

Kaar Kaalam : (Aavani, Purattasi)

Koothir Kaalam : (Ayppasi, Karthigai)

Munpani Kaalam : (Maarkazhi, Thai)

Pinpani Kaalam : (Maasi, Panguni)

Elavenil Kaalam : (Chittirai, Vaikasi)

Mudhuvenil Kaalam : (Aani, Aadi)

3. UDAL: 4

Vali Udal

Azhal Udal

Iya Udal

Kalappu Udal

4. KANMENTHIRIYANGAL: 5

Vaai

Kaal

Kai

Eruvai

Karuvai

5. PORI / PULANGAL: 5

Mei - Ooru

Vaai - Suvai

Kann - Oli

Mookku - Nattram

Sevi - Osai

6. GUNAM: 3

Sathuva Gunam

Rajo Gunam

Thamo Gunam

7. UDAL KATTUGAL: 7

Saaram

Senneer

Oon

Kozhuppu

Enbu

Moolai

Sukkilam / Suronitham

8. MALAM: 3

Malam

Moothiram

Viyarvai

9. MUKKUTRANGAL

VALI

Piraanan

Abaanan

Uthaanan

Viyaanan

Samaanan

Nagan

Koorman

Kirukaran

Devathathan

Thananjeyan

AZHAL

Anala Pitham

Ranjaga Pitham

Aalosaga Pitham

Praasaga Pitham

Saathaga Pitham

IYAM

Avalambakam

Kilethagam

Pothagam

Tharpagam

Santhigam

10. ENVAGAI THERVU

Naadi

Sparisam

Naa

Niram

Mozhi

Vizhi

Malam

Niram

Irugal

Ilagal

Moothiram

Neerkuri:

Niram

Edai

Manam

Nurai

Enjal

Neikuri:

SIGNS AND SYMPTOMS

1. Irregular menstruation
2. Oligomenorrhoea
3. Dysmenorrhoea
4. Hirsutism
5. Acanthosis nigricans

INVESTIGATION

A)BLOOD INVESTIGATIONS:

BLOOD INVESTIGATIONS		**BEFORE TREATMENT**	**AFTER TREATMENT**
Hb (gms/dl)			
T.RBC (millions cells/cu.mm)			
ESR (mm)	½ hr		
	1 hr		
T.WBC (cells/cu.mm)			
Differential Count (%)	Polymorphs		
	Lymphocytes		
	Monocytes		
	Eosinophils		
	Basophils		
Blood Sugar (R) mg/dl			
Serum Cholesterol (mg/dl)			

B) URINE INVESTIGATIONS:

URINE INVESTIGATIONS	BEFORE TREATMENT	AFTER TREATMENT
Albumin		
Sugar		
Deposits		

C) SPECIFIC INVESTIGATIONS:

USG- Whole Abdomen

Follicular Study

D)BODYMASS INDEX (BMI)

SIGN AND SYMPTOMS:

S.No	CLINICAL FEATURES	BEFORE TREATMENT	AFTER TREATMENT		
			1st cycle	2nd cycle	3rd cycle
1	Regularity of cycle				
2	Length of cycle				
3	Duration of flow				
4	Level of flow				
5	Abdominal pain				
6	Low back pain				
7	Hirsutism				
8	Acanthosis nigricans				

DIAGNOSIS

SOOTHAGA VAAYU (POLYCYSTIC OVARIAN SYNDROME)

TRIAL DRUG : KALINGATHI ENNAI

DOSE : 15ml

Anubanam: WARM WATER

Duration of Treatment : 3 consecutive menstrual cycles

BIBLIOGRAPHY

BIBILIOGRAPHY

1.Siddha Medicine, Encyclopaedia Britania, Last updated 8-25-2014.

2.Antiquity of Siddha system, Indhiya maruthuvam and homeopathy eyakkam, Chennai 1st Edition, pg.14.

3.Shanmugavelu M, Sathaga nadi, Noi Nadal Noi Mudhal Nadal Thirattu, Part-1, Indian Medicine and Homepathy, Fourth Edition 2006, pg.92.

4."How many people are affected or at risk for PCOS?" http:www.nichd.nih.gov, 2013-05-23, retrieved 13March 2015.

5.VOS T Flaxman AD, et al (2012), "Years lived with disability (YLD) for 1160 sequelae of 289 disease and injuries 1990-2010; a systematic analysis for the Global Burden of Disease Study 2010". Lancet 380 (9859) : 2163-96.

6.Definition of Siddha Medicine, Medicine Net.com, Dec 25, 2014, Last editorial Review 9/20/12.

7. Sambasivam Pillai TV, Dictionary based on Indian Medical Science, Dept. of Indian Medicine & Homeopathy, Chennai- 106, 2nd Edition, March 1998, pg.372-373.

8.Mohanaraj T, Arivaiyar Chinthamani, A.T.S.V.S Siddha medical College and Hospital, Munjirai, 1st Edition, May 2008, pg.220-221.

9. Mohanaraj T, Arivaiyar Chinthamani, A.T.S.V.S Siddha medical College and Hospital, Munjirai, 1st Edition, May 2008, pg.24.

10.Venkatarajan S, Dhanwanthri Vaidhyam Part-1, Director, Saraswathi mahal library, Thanjavur, 3rd Edition, 2006, pg.251.

11.Venkatarajan S, Agathiyar Kanma Kaandam 300, Thamarai library, Chennai, 1st Edition, June 1995, pg.33.

12.Kanthasami MV, Pathinen Siddhar Aruliya Aaviyalikum Amudhamurai Churrukam, Arulmigu Pazhani Dhandayuthapaani Swami Thirukovil Siddha Maruthuvanool veliettukkuzhu, 2nd Edition, 1975, pg.290.

13. Mohanaraj T, Arivaiyar Chinthamani, A.T.S.V.S Siddha medical College and Hospital, Munjirai, 1st Edition, May 2008, pg.244.

14. Mohanaraj T, Arivaiyar Chinthamani, A.T.S.V.S Siddha medical College and Hospital, Munjirai, 1st Edition, May 2008, pg.160.

15.Kalathur KM, Pathinen Siddharkal aruliseidha Naadi Sasthiram, 2013, pg.191.

16.Ramachandran SP, Agathiyar Vaidhiya Kaaviyam 1500, Thamarai Noolagam, Chennai-26, 1st Edition, July 1992, pg.32.

17. Ramachandran SP, Thirumoolar Karukkadai Vaithyam 600, Thamarai Noolagam, Chennai-26, 1st Edition, July 1992, pg.48.

18.Marudhamuthu K, Brammamuni Vaidhiya Suthiram-390, Director, Saraswathi mahal library, Thanjavur, 2nd Edition, Sep 2005, pg.93-94.

19.Ramachandran SP, Thirumoolar Karukkadai Vaithiyam 600, Thamarai Noolagam, Chennai-26, 2nd Edition, Feb 1998, pg.47.

20.Kalathur Kandhasami Mudhaliyar, Pathinensiddharkal padiya vaithiya sillarai kovai, part 1, Thamarai Library, Apr 1994, pg.4.

21.Kanthasami V Mudhaliyar, Pathinensiddhar aruliya Aaviyalikum Amudhamurai Churrukam, Arulmigu Pazhani Dhandayuthapaani Swami Thirukovil Siddha Maruthuvanool veliettukkuzhu, 2nd Edition, 1975, pg.241.

22.Venkattarajan S, Dhanwanthri Vaidhyam part-1, 3rd Edition,2006, pg.61.

23.Venkatarajan S, Dhanwanthri Vaidhyam Part-1, Director, Saraswathi Mahal Library, Thanjavur, 3rd Edition, 2006, pg.241.

24.Kanthasami V Mudhaliyar, Aathmaratchamirthamenum Vaithiya Sara Sangiragam, 1st Edition, Thamarai Library, Apr 1996, pg.49.

25.Kanthasami V Mudhaliyar, Sarabenthirar Vaithiya Muraigal, 1st Edition, Saraswathi mahal library, Thanjavur, pg.245.

26.Shanmugavelu M, Noi Nadal Noi Mudhal Nadal Thirattu, Indian Medicine and Homeopathy, Fourth Edition 2006, pg.97.

27.Uthamarayan KS, Siddha Maruthuvanga Surukkam, Indian Medicine and Homeopathy, Third Edition 2003, pg.136.

28.Uthamarayan KS, Siddha Maruthuvanga Surukkam, Indian Medicine and Homeopathy, Third Edition 2003, pg.28.

29.Uthamarayan KS, Siddha Maruthuvanga Surukkam, Indian Medicine and Homeopathy, Third Edition 2003, pg.140.

30. Uthamarayan KS, Siddha Maruthuvanga Surukkam, Indian Medicine and Homeopathy, Third Edition 2003, pg.154.

31. Uthamarayan KS, Siddha Maruthuvanga Surukkam, Indian Medicine and Homeopathy, Third Edition 2003, pg.159.

32. Kanusamipillai C, Sikitcha Rathna Deepam Ennum Vaidhiya Nool, B.Rathna Nayakar and sons, 2011, pg.1.

33.Theraiyar, Theraiyar Yamaga Venba, Indian Medicine and Homeopathy Department, 1975, pg.11.

34. Shanmugavelu M, Noi Nadal Noi Mudhal Nadal Thirattu, Part-1, Indian Medicine and Homeopathy, Fourth Edition 2006, pg.270.

35. Kannusamipillai, Sikitcha Rathna Deepam Ennum Vaidhiya Nool, B. Rathna nayakkar and sons 2011, pg.7.

36. Shanmugavelu M, Noi Nadal Noi Mudhal Nadal Thirattu, Part-1, Indian Medicine and Homeopathy, Fourth Edition 2006, pg.139.

37. Shanmugavelu M, Noi Nadal Noi Mudhal Nadal Thirattu, Part-1, Indian Medicine and Homeopathy, Fourth Edition 2006, pg- Shanmugavelu M, Noi Nadal Noi Mudhal Nadal Thirattu, Part-1, Indian Medicine and Homeopathy, Fourth Edition 2006, pg.270.

38. Shanmugavelu M, Noi Nadal Noi Mudhal Nadal Thirattu, Part-1, Indian Medicine and Homeopathy, Fourth Edition 2006, pg.173.

39. Kalathur KM, Pathinen Siddharkal aruliseidha Naadi Sasthiram, 2013, pg.42.

40. Kalathur KM, Pathinen Siddharkal aruliseidha Naadi Sasthiram, 2013, pg.42.

41. Kannusamipillai, Sikitcha Rathna Deepam Ennum Vaidhiya Nool, B. Rathna nayakkar and sons 2011, pg.7.

42. Shanmugavelu M, Noi Nadal Noi Mudhal Nadal Thirattu, Part-1, Indian Medicine and Homeopathy, Fourth Edition 2006, pg.282.

43. Shanmugavelu M, Noi Nadal Noi Mudhal Nadal Thirattu, Part-1, Indian Medicine and Homeopathy, Fourth Edition 2006, pg.293.

44. Uthamarayan KS, Siddha Maruthuvanga Surukkam, Indian Medicine and Homeopathy, Third Edition 2003, pg.52.

45. Dutta Roys, Yogic Exercises, Jaypee Publications, pg.220-240.

46. Gyton & Hall, Textbook of Medical Physiology, W.B.Sausders company, 9th Edition, pg.1022,1023.

47. B.D.Chaurasia's, Human anatomy, CBS Publishers and Distributors, New Delhi, Fourth Edition, 2004, pg.353-360.

48. Losos, Jonathan B; Raven, Peter H; Johnson, George B; Singer, Suan R.(2002) Biology, New York; MC Graw-Hill, ISBN 0-07-303120-8, pg.1207-1209.

49. Menstruation and the Menstrual cycle, Womens health.gov. April 2007, Archeived from the original on 24 october 2008.

50. Leatz, Gretcher; Lobo, Rogerio A; Gerhenson et,al (2013), Comprehensive gynaecology, St.Louis; Elsevier Mosby, ISBN 978-0-323-06986-1, Retrieved April 2012.

51. Gray, Hentry David (2000), The Ovum, Anatomy of the human body, Philadelphia; Bartleyby.com, ISBN 1-58734-102-6, Retrieved 5 oct 2008.

52. K.Sembulingam, Essentials of Medical Physiology, Jaypee brothers, New delhi, Fourth Edition 2006, pg.445-446.

53. K.Sembulingam, Essentials of Medical Physiology, Jaypee brothers, New delhi, Fourth Edition 2006, pg.448.

54. K.Sembulingam, Essentials of Medical Physiology, Jaypee brothers, New delhi, Fourth Edition 2006, pg.438-441.

55. K.Sembulingam, Essentials of Medical Physiology, Jaypee brothers, New delhi, Fourth Edition 2006, pg.424-426.

56. Revised 2003 consensus on diagnostic criteria and long term health risks related to polycystic ovary syndrome, Fertile Steril 2004, 81; pg.19-25.

57. Jacqueline Boyle, Helena J Teede, Polycystic ovary syndrome, An update volume 41, No. 10, October 2012, pg.752-756.

58. Harshmohan, MD, Textbook of Pathology, Jaypee brothers, New Delhi, 2nd Edition, March 1994, pg.754-755.

59. DC Dutta, Textbook of Gynaecology, New central book agency (p) ltd, Calcutta, 2nd Edition- 1994, pg.409-412.

60. Howkins & Bourne, Shaw's Textbook of Gynaecology, B.I. Churchuil Livingstone (p) ltd, New Delhi, 11th Edition, 1994, pg.439.

61. Kannusami pillai, Sikicharathnadeepam irandam pagamagiya vaidhiya chinthamani, Rathna nayakar sons,2012, pg.185-186.

62. Murugesa Muthaliyar, Siddha Materia Medica,Indian Medicine & Homeopathy Department, Chennai-106, 6th Edition 2006, pg.90-91.

63. Murugesa Muthaliyar, Siddha Materia Medica,Indian Medicine & Homeopathy Department, Chennai-106, 6th Edition 2006, pg.833-834.

64. Murugesa Muthaliyar, Siddha Materia Medica,Indian Medicine & Homeopathy Department, Chennai-106, 6th Edition 2006, pg.158-160.

65. Murugesa Muthaliyar, Siddha Materia Medica,Indian Medicine & Homeopathy Department, Chennai-106, 6th Edition 2006, pg.72-73.

66. Murugesa Muthaliyar, Siddha Materia Medica,Indian Medicine & Homeopathy Department, Chennai-106, 6th Edition 2006, pg.98-101.

67. Murugesa Muthaliyar, Siddha Materia Medica,Indian Medicine & Homeopathy Department, Chennai-106, 6th Edition 2006, pg.459-462.

68. Murugesa Muthaliyar, Siddha Materia Medica,Indian Medicine & Homeopathy Department, Chennai-106, 6th Edition 2006, pg.389-391.

69. Murugesa Muthaliyar, Siddha Materia Medica,Indian Medicine & Homeopathy Department, Chennai-106, 6th Edition 2006, pg.421-423.

70. Murugesa Muthaliyar, Siddha Materia Medica,Indian Medicine & Homeopathy Department, Chennai-106, 6th Edition 2006, pg.111-113.

71. Murugesa Muthaliyar, Siddha Materia Medica,Indian Medicine & Homeopathy Department, Chennai-106, 6th Edition 2006, pg.113-115.

72. Murugesa Muthaliyar, Siddha Materia Medica,Indian Medicine & Homeopathy Department, Chennai-106, 6th Edition 2006, pg.720-722.

73. Murugesa Muthaliyar, Siddha Materia Medica,Indian Medicine & Homeopathy Department, Chennai-106, 6th Edition 2006, pg.165-167.